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 NEWS  7  DEC 21  IPC search and display fields enhanced in CA/CAplus with the
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 NEWS  8  DEC 23  New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                  USPAT2
 NEWS  9  JAN 13  IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS 10  JAN 13  New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
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 NEWS 11  JAN 17  Pre-1988 INPI data added to MARPAT
 NEWS 12  JAN 17  IPC 8 in the WPI family of databases including WPIFV
 NEWS 13  JAN 30  Saved answer limit increased
 NEWS 14  JAN 31  Monthly current-awareness alert (SDI) frequency
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 NEWS 15  FEB 21  STN AnaVist, Version 1.1, lets you share your STN AnaVist
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 NEWS 16  FEB 22  Status of current WO (PCT) information on STN
 NEWS 17  FEB 22  The IPC thesaurus added to additional patent databases on STN
 NEWS 18  FEB 22  Updates in EPFULL; IPC 8 enhancements added
 NEWS 19  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS 20  FEB 28  MEDLINE/LMEDLINE reload improves functionality
 NEWS 21  FEB 28  TOXCENTER reloaded with enhancements
 NEWS 22  FEB 28  REGISTRY/ZREGISTRY enhanced with more experimental spectral
                  property data
 NEWS 23  MAR 01  INSPEC reloaded and enhanced
 NEWS 24  MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
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FILE 'HOME' ENTERED AT 15:39:03 ON 06 MAR 2006

=> file uspatful
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'USPATFULL' ENTERED AT 15:39:18 ON 06 MAR 2006
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Mar 2006 (20060302/PD)
FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)
HIGHEST GRANTED PATENT NUMBER: US7007305
HIGHEST APPLICATION PUBLICATION NUMBER: US2006048257
CA INDEXING IS CURRENT THROUGH 28 Feb 2006 (20060228/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Mar 2006 (20060302/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005


=> s (fowlpox/clm or TROVAC/clm)
          116 FOWLPOX/CLM
           12 TROVAC/CLM
L1        116 (FOWLPOX/CLM OR TROVAC/CLM)
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      3006106 AY<2000
L2          53 L1 AND AY<2000

=> s l2 and (HIV/clm or Gag/clm)
         6413 HIV/CLM
         1283 GAG/CLM
L3           6 L2 AND (HIV/CLM OR GAG/CLM)

=> d l3,cbib,1-6

L3   ANSWER 1 OF 6  USPATFULL on STN
2002:340150 Recombinant swinepox virus.
    Cochran, Mark D., Carlsbad, CA, United States
    Junker, David E., San Diego, CA, United States
    Syntro Corporation, San Diego, CA, United States (U.S. corporation)
    US 6497882 B1 20021224
    APPLICATION: US 1995-472679  19950607 (8)
    DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3   ANSWER 2 OF 6  USPATFULL on STN
2001:116789 Direct molecular cloning of foreign genes into poxviruses and
    methods for the preparation of recombinant proteins.
    Dorner, Friedrich, Vienna, Austria
    Scheiflinger, Friedrich, Orth/Donau, Austria
    Falkner, Falko Gunter, Mannsdorf, Austria
    Pfleiderer, Michael, Breitstetten, Austria
    Baxter Aktiengesellschaft, Vienna, Australia (non-U.S. corporation)
    US 6265183 B1 20010724
    APPLICATION: US 1994-358928  19941219 (8)
    DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3   ANSWER 3 OF 6  USPATFULL on STN
2000:105429 Methods for generating immune responses employing modified vaccinia
    of fowlpox viruses.
    Dorner, Friedrich, Vienna, Austria
    Scheiflinger, Friedrich, Orth/Donau, Austria
    Falkner, Falko Gunter, Mannsdorf, Austria
    Pfleiderer, Michael, Breitstetten, Austria
    Immuno AG., Vienna, Austria (non-U.S. corporation)
    US 6103244 20000815
    APPLICATION: US 1996-651472  19960522 (8)
    DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3   ANSWER 4 OF 6  USPATFULL on STN
1999:81550 Recombinant fowlpox viruses and uses thereof.
    Cochran, Mark D., Carlsbad, CA, United States
    Junker, David E., San Diego, CA, United States
    Syntro Corporation, Lenexa, KS, United States (U.S. corporation)
    US 5925358 19990720
    APPLICATION: US 1995-484575  19950607 (8)
    DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3   ANSWER 5 OF 6  USPATFULL on STN
1998:108035 Self assembled, defective, nonself-propagating viral particles.
    Mazzara, Gail P., Winchester, MA, United States
    Panicali, Dennis L., Acton, MA, United States
    Roberts, Bryan, Cambridge, MA, United States
    Gritz, Linda R., Somerville, MA, United States
    Stallard, Virginia, Seattle, WA, United States
    Therion Biologics Corporation, Cambridge, MA, United States (U.S.
    corporation)
    US 5804196 19980908
    APPLICATION: US 1995-481031  19950607 (8)
    DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3   ANSWER 6 OF 6  USPATFULL on STN
97:42784 Self assembled, defective, non-self-propagating lentivirus particles.
    Mazzara, Gail P., Winchester, MA, United States
    Panicali, Dennis L., Acton, MA, United States
    Roberts, Bryan, Cambridge, MA, United States
    Gritz, Linda R., Somerville, MA, United States
    Stallard, Virginia, Sequim, WA, United States
    Mahr, Anna, Natick, MA, United States
    Therion Biologics, Incorporated, Cambridge, MA, United States (U.S.
    corporation)
    US 5631154 19970520
    APPLICATION: US 1993-18344  19930216 (8)
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 13,cbib,ab,clm,1-6

L3 ANSWER 1 OF 6 USPATFULL on STN
2002:340150 Recombinant swinepox virus.
Cochran, Mark D., Carlsbad, CA, United States
Junker, David E., San Diego, CA, United States
Syntro Corporation, San Diego, CA, United States (U.S. corporation)
US 6497882 B1 20021224
APPLICATION: US 1995-472679 19950607 (8)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a recombinant swinepox virus comprising a foreign DNA sequence inserted into the swinepox virus genomic DNA, wherein the foreign DNA sequence is inserted within a HindIII K fragment of the swinepox virus genomic DNA and is capable of being expressed in a swinepox virus infected host cell.

The invention further provides homology vectors, vaccines and methods of immunization.
CLM What is claimed is:
1. A recombinant swinepox virus comprising a foreign DNA inserted into a swinepox virus genome, wherein the foreign DNA is inserted within a region corresponding to a 3.2 kB subfragment which contains a HindIII site and an EcoRI site within the HindIII K fragment of the swinepox virus genome and is capable of being expressed in a host cell into which the virus is introduced.

2. The recombinant swinepox virus of claim 1, wherein the foreign DNA is inserted into an open reading frame within the region corresponding to the 3.2 kB subfragment.

3. The recombinant swinepox virus of claim 2, wherein the foreign DNA is inserted into a B18R gene.

4. The recombinant swinepox virus of claim 2, wherein the foreign DNA is inserted into a B4R gene.

5. The recombinant swinepox virus of claim 1, wherein the foreign DNA encodes a polypeptide.

6. The recombinant swinepox virus of claim 5, wherein the polypeptide is antigenic.

7. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from a virus which is selected from the group consisting of: human herpesvirus, herpes simplex virus-1, herpes simplex virus-2, human cytomegalovirus, Epstein-Barr virus, varicella-zoster virus, human herpesvirus-6, human herpesvirus-7, human influenza, human immunodeficiency virus, rabies virus, measles virus, hepatitis B virus, and hepatitis C virus.

8. The recombinant swinepox virus of claim 5, wherein the polypeptide is hepatitis B virus core protein or hepatitis B virus surface protein.

9. The recombinant swinepox virus of claim 5, wherein the polypeptide is equine influenza virus neuraminidase or equine influenza virus hemagglutinin.

10. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: equine influenza virus type A/Alaska 91 neuraminidase, equine influenza virus type A/Kentucky 92 neuraminidase, equine influenza virus type A/Prague 56 neuraminidase, equine influenza virus type A/Miami 63 neuraminidase, equine influenza virus type A/Kentucky 81 neuraminidase, equine herpesvirus type 1 glycoprotein B, and equine herpesvirus type 1 glycoprotein D.

11. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: hog cholera virus glycoprotein E1, hog cholera virus glycoprotein E2, swine influenza virus hemagglutinin, swine influenza virus neuraminidase, swine influenza virus matrix, swine influenza virus nucleoprotein, pseudorabies virus glycoprotein B, pseudorabies virus glycoprotein C, pseudorabies virus glycoprotein D, and PRRS virus ORF7.

12. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: Infectious bovine rhinotracheitis virus gE, bovine respiratory syncytial virus attachment protein (BRSV G), bovine respiratory syncytial virus fusion protein (BRSV F), bovine respiratory syncytial virus nucleocapsid protein (BRSV

parainfluenza virus type 3 hemagglutinin neuraminidase.

13. The recombinant swinepox virus of claim 5, wherein the polypeptide is bovine viral diarrhea virus (BVDV) glycoprotein 48 or bovine viral diarrhea virus glycoprotein 53.

14. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: feline immunodeficiency virus **gag**, feline immunodeficiency virus env, infectious laryngotracheitis virus glycoprotein B, infectious laryngotracheitis virus glycoprotein I, infectious laryngotracheitis virus glycoprotein D, infectious bovine rhinotracheitis virus glycoprotein G, infectious bovine rhinotracheitis virus glycoprotein E, pseudorabies virus glycoprotein 50, pseudorabies virus II glycoprotein B, pseudorabies virus III glycoprotein C, pseudorabies virus glycoprotein E, pseudorabies virus glycoprotein H, Marek's disease virus glycoprotein A, Marek's disease virus glycoprotein B, Marek's disease virus glycoprotein D, Newcastle disease virus hemagglutinin, Newcastle disease virus neuraminidase, Newcastle disease virus fusion, infectious bursal disease virus VP2, infectious bursal disease virus VP3, infectious bursal disease virus VP4, infectious bursal disease virus polyprotein, infectious bronchitis virus spike, and infectious bronchitis virus matrix.

15. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from an organism selected from the group consisting of Streptococcus equi, equine infectious anemia virus, equine encephalitis virus, equine rhinovirus and equine rotavirus.

16. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from an organism selected from the group consisting of avian encephalomyelitis virus, avian reovirus, avian paramyxovirus, avian influenza virus, avian adenovirus, **fowlpox** virus, avian coronavirus, avian rotavirus, chick anemia virus, Salmonella spp., E. coli, Pasteurella spp., Bordetella spp., Eimeria spp., Histomonas spp., Trichomonas spp., poultry. nematodes, cestodes, trematodes, poultry mites, poultry lice and poultry protozoa.

17. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from an organism selected from the group consisting of canine herpesvirus, canine distemper virus, canine adenovirus type 1, canine adenovirus type 2, parainfluenza virus, Leptospira canicola, parvovirus, coronavirus, Borrelia burgdorferi, canine herpesvirus, Bordetella bronchiseptica, Dirofilaria immitis and rabies virus.

18. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from a virus selected from the group consisting of feline leukemia virus, feline immunodeficiency virus, feline herpesvirus and feline infectious peritonitis virus.

19. The recombinant swinepox virus of claim 1, further comprising a foreign DNA which encodes a detectable marker.

20. The recombinant swinepox virus of claim 19, wherein the detectable marker is E. coli beta-galactosidase.

21. The recombinant swinepox virus of claim 19, wherein the detectable marker is E. coli beta-glucuronidase.

22. The recombinant swinepox virus of claim 1, wherein the foreign DNA encodes a cytokine.

23. The recombinant swinepox virus of claim 22, wherein the cytokine is chicken myelomonocytic growth factor (cMGF) or chicken interferon (cIFN).

24. The recombinant swinepox virus of claim 22, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-6, interleukin-12, interferons, and granulocyte-macrophage colony stimulating factor.

25. The recombinant swinepox virus of claim 1, wherein the foreign DNA is under the control of an endogenous poxvirus promoter.

26. The recombinant swinepox virus of claim 1, wherein the foreign DNA is under the control of a heterologous promoter.

27. The recombinant swinepox virus of claim 1, wherein the promoter is: pox synthetic late promoter 1, pox synthetic late promoter 2 early promoter 2, pox O1L promoter, pox I4L promoter, pox I3L promoter, pox I2L promoter, pox I1L promoter, or pox E10R promoter.

28. A vaccine which comprises an effective immunizing amount of the

29. A method of immunizing an animal against an animal pathogen which comprises administering to the animal an effective immunizing dose of the vaccine of claim 28.

30. A homology vector for producing a recombinant swinepox virus by inserting foreign DNA into a swinepox virus genome which comprises a double-stranded DNA consisting essentially of: a) double stranded foreign DNA not usually present within the swinepox virus genome; b) at one end the foreign DNA, double-stranded swinepox virus DNA homologous to the virus genome located at one side of the HindIII K fragment of the coding region of the swinepox virus genome; and c) at the other end of the foreign DNA, double-stranded swinepox virus DNA homologous to the virus genome located at the other side of the HindIII K fragment of the coding region of the swinepox virus genome.

31. The homology vector of claim 30, wherein the foreign DNA encodes a cytokine.

32. The homology vector of claim 31, wherein the cytokine is chicken myelomonocytic growth factor (cMGF) or chicken interferon (cIFN).

33. The homology vector of claim 30, wherein the foreign DNA encodes a polypeptide.

34. A homology vector of claim 33, wherein the polypeptide is antigenic.

35. The homology vector of claim 30, wherein the foreign DNA is under control of a promoter.

L3 ANSWER 2 OF 6 USPATFULL on STN
2001:116789 Direct molecular cloning of foreign genes into poxviruses and methods for the preparation of recombinant proteins.
Dorner, Friedrich, Vienna, Austria
Scheiflinger, Friedrich, Orth/Donau, Austria
Falkner, Falko Gunter, Mannsdorf, Austria
Pfleiderer, Michael, Breitstetten, Austria
Baxter Aktiengesellschaft, Vienna, Australia (non-U.S. corporation)
US 6265183 B1 20010724
APPLICATION: US 1994-358928 19941219 (8)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is disclosed for producing a modified eukaryotic cytoplasmic DNA virus by direct molecular cloning of a modified DNA molecule comprising a modified cytoplasmic DNA virus genome. The inventive method comprises the steps of (I) modifying under extracellular conditions a DNA molecule comprising a first cytoplasmic DNA virus genome to produce a modified DNA molecule comprising the modified cytoplasmic DNA virus genome; (II) introducing the modified DNA molecule into a first host cell which packages the modified DNA molecule into infectious virions; and (III) recovering from the host cell virions comprised of the modified viral genome. The host cell is infected with a helper virus which is expressed to package the modified viral genome into infectious virions. Examples of packaging a modified poxvirus genome by a helper poxvirus of the same or different genus are described. Also disclosed are novel poxvirus vectors for direct molecular cloning of open reading frames into a restriction enzyme cleavage site that is unique in the vector. In one model poxvirus vector, the open reading frame is transcribed by a promoter located in the vector DNA upstream of a multiple cloning site comprised of several unique cleavage sites.
CLM What is claimed:
1. A method for producing a protein employing a modified vaccinia viral expression system comprising the following steps: (a) providing a modified vaccinia virus containing a heterologous insert encoding a protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site; (b) infecting a vertebrate cell culture with the modified vaccinia virus from step (a); (c) culturing the infected cells under conditions resulting in expression of the protein; and, (d) isolating the protein produced by the infected cells.

2. The method according to claim 1, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

3. The method according to claim 1, wherein the protein is selected from the group consisting of prothrombin, Factor IX, Protein S, von Willebrand Factor, lys-plasminogen, and glu-plasminogen.

4. The method according to claim 1, wherein the restriction endonuclease is selected from the group consisting of NotI, SmaI, ApaI, and RsrII.

expression system comprising the following steps: (a) providing a modified **fowlpox** virus containing a heterologous insert encoding a protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII; (b) infecting a vertebrate cell culture with the modified vaccinia virus from step (a); (c) culturing the infected cells under conditions resulting in expression of the protein; and, (d) isolating the protein produced by the infected cells.

6. The method according to claim 5, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

7. The method according to claim 5, wherein the protein is selected from the group consisting of prothrombin, Factor IX, Protein S, von Willebrand Factor, lys-plasminogen, and glu-plasminogen.

8. A method for producing a protein employing a modified vaccinia viral expression system comprising the following steps: (a) infecting cells with a modified vaccinia virus containing a heterologous insert encoding a protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site; (b) culturing the infected cells from step (a) under conditions resulting in expression of the protein.

9. The method according to claim 8, further comprising isolating the protein produced by the infected cells of step (b).

10. The method according to claim 8, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

11. The method according to claim 8, wherein the protein is a human blood protein.

12. The method according to claim 11, wherein the human blood protein is selected from the group consisting of prothrombin, Factor IX, Protein S, von Willebrand Factor, lys-plasminogen, and glu-plasminogen.

13. A method for producing a protein employing a modified **fowlpox** viral expression system comprising the following steps: (a) infecting cells with a modified **fowlpox** virus containing a heterologous insert encoding a protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII; and, (b) culturing the infected cells from step (a) under conditions resulting in expression of the protein.

14. The method according to claim 13, further comprising isolating the protein produced by the infected cells of step (b).

15. The method according to claim 13, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

16. The method according to claim 13, wherein the protein is a human blood protein.

17. The method according to claim 16, wherein the human blood protein is selected from the group consisting of prothrombin, Factor IX, Protein S, von Willebrand Factor, lys-plasminogen, and glu-plasminogen.

L3 ANSWER 3 OF 6 USPATFULL on STN
2000:105429 Methods for generating immune responses employing modified vaccinia of fowlpox viruses.
Dorner, Friedrich, Vienna, Austria
Scheiflinger, Friedrich, Orth/Donau, Austria
Falkner, Falko Gunter, Mannsdorf, Austria
Pfleiderer, Michael, Breitstetten, Austria
Immuno AG., Vienna, Austria (non-U.S. corporation)
US 6103244 20000815
APPLICATION: US 1996-651472 19960522 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is disclosed for producing a modified eukaryotic cytoplasmic DNA virus by direct molecular cloning of a modified DNA molecule comprising a modified cytoplasmic DNA virus genome. The inventive method comprises the steps of (I) modifying under extracellular conditions a DNA molecule comprising a first cytoplasmic DNA virus genome to produce a modified DNA molecule comprising the modified cytoplasmic DNA virus genome; (II) introducing the modified DNA molecule into a first host

and (III) recovering from the host cell virions comprised of the modified viral genome. The host cell is infected with a helper virus which is expressed to package the modified viral genome into infectious virions. Examples of packaging a modified poxvirus genome by a helper poxvirus of the same or different genus are described. Also disclosed are novel poxvirus vectors for direct molecular cloning of open reading frames into a restriction enzyme cleavage site that is unique in the vector. In one model poxvirus vector, the open reading frame is transcribed by a promoter located in the vector DNA upstream of a multiple cloning site comprised of several unique cleavage sites.

CLM What is claimed is:

1. A method for generating an immune response in a vertebrate against a heterologous protein comprising the following steps: (a) providing a modified vaccinia virus containing a heterologous insert encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site; (b) administering the modified vaccinia virus to the vertebrate in an amount sufficient to generate the immune response.

2. The method according to claim 1, wherein the protein is a viral protein.

3. The method according to claim 2, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

4. The method according to claim 1, wherein the cleavage site is recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII.

5. A method for priming an immune response in a vertebrate comprising the following steps: (a) providing a modified vaccinia virus containing a heterologous insert encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site; (b) administering the modified vaccinia virus to the vertebrate in an amount sufficient to prime the immune response.

6. The method according to claim 5, wherein the protein is a viral protein.

7. The method according to claim 6, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

8. The method according to claim 5, wherein the cleavage site is recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII.

9. A method for generating an immune response in a vertebrate against a heterologous protein comprising the following steps: (a) providing a modified **fowlpox** virus containing a heterologous insert encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII; (b) administering the modified **fowlpox** virus to the vertebrate in an amount sufficient to generate the immune response.

10. The method according to claim 9, wherein the protein is a viral protein.

11. The method according to claim 10, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

12. A method for priming an immune response in a vertebrate against a heterologous protein comprising the following steps: (a) providing a modified **fowlpox** virus containing a heterologous insert encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII; (b) administering the modified **fowlpox** virus to the vertebrate in an amount sufficient to prime the immune response.

13. The method according to claim 12, wherein the protein is a viral protein.

14. The method according to claim 13, wherein the protein is selected from the group consisting of **HIV** gp160, **HIV Gag**, and **HIV Gag**-Pol.

L3 ANSWER 4 OF 6 USPATFULL on STN
1999:81550 Recombinant fowlpox viruses and uses thereof.

Junker, David E., San Diego, CA, United States
Syntro Corporation, Lenexa, KS, United States (U.S. corporation)
US 5925358 19990720
APPLICATION: US 1995-484575 19950607 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a recombinant fowlpox virus comprising a foreign DNA sequence inserted into the fowlpox virus genomic DNA, wherein the foreign DNA sequence is inserted within a 2.8 kB EcoRI fragment of the fowlpox virus genomic DNA and is capable of being expressed in a fowlpox virus infected host cell. The invention further provides homology vectors, vaccines and methods of immunization.

CLM What is claimed is:

1. A recombinant **fowlpox** virus comprising a foreign DNA inserted into a **fowlpox** virus genome, wherein the foreign DNA is inserted within a region corresponding to a 2.8 kB EcoRI fragment of the **fowlpox** virus genome and is capable of being expressed in a host cell into which the virus is introduced.

2. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is inserted within a SnaBI site within the region which corresponds to the 2.8 kB EcoRI fragment.

3. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA encodes a polypeptide.

4. The recombinant **fowlpox** virus of claim 3, wherein the polypeptide is antigenic.

5. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is hepatitis B virus core protein or hepatitis B virus surface protein.

6. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is equine influenza virus neuraminidase or hemagglutinin.

7. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is selected from the group consisting of: equine influenza virus type A/Alaska 91 neuraminidase, equine influenza virus type A/Kentucky 92 neuraminidase, equine influenza virus type A/Prague 56 neuraminidase, equine influenza virus type A/Miami 63 neuraminidase, equine influenza virus type A/Kentucky 81 neuraminidase, equine herpesvirus type 1 glycoprotein B, and equine herpesvirus type 1 glycoprotein D.

8. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is selected from the group consisting of: hog cholera virus glycoprotein E1, hog cholera virus glycoprotein E2, swine influenza virus hemagglutinin, neuraminidase, matrix and nucleoprotein, pseudorabies virus glycoprotein B, glycoprotein C and glycoprotein D, and PRRS virus ORF7.

9. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is selected from the group consisting of: Infectious bovine rhinotracheitis virus gE, bovine respiratory syncytial virus attachment protein (BRSV G), bovine respiratory syncytial virus fusion protein (BRSV F), bovine respiratory syncytial virus nucleocapsid protein (BRSV N), bovine parainfluenza virus type 3 fusion protein, and the bovine parainfluenza virus type 3 hemagglutinin neuraminidase.

10. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is bovine viral diarrhea virus (BVDV) glycoprotein 48 or glycoprotein 53.

11. The recombinant **fowlpox** virus of claim 4, wherein the foreign DNA sequence encodes an antigenic polypeptide which is selected from the group consisting of: feline immunodeficiency virus **gag**, feline immunodeficiency virus env, infectious laryngotracheitis virus glycoprotein B, infectious laryngotracheitis virus glycoprotein I, infectious laryngotracheitis virus glycoprotein D, infectious bovine rhinotracheitis virus glycoprotein G, infectious bovine rhinotracheitis virus glycoprotein E, pseudorabies virus glycoprotein 50, pseudorabies virus II glycoprotein B, pseudorabies virus III glycoprotein C, pseudorabies virus glycoprotein E, pseudorabies virus glycoprotein H, marek's disease virus glycoprotein A, marek's disease virus glycoprotein B, marek's disease virus glycoprotein D, newcastle disease virus hemagglutinin or neuraminadase, newcastle disease virus fusion, infectious bursal disease virus VP2, infectious bursal disease virus VP3, infectious bursal disease virus VP4, infectious bursal disease virus polyprotein, infectious bronchitis virus spike, infectious bronchitis virus matrix, and chick anemia virus.

foreign DNA sequence which encodes a detectable marker.

13. The recombinant **fowlpox** virus of claim 12, wherein the detectable marker is E. coli beta-galactosidase.

14. The recombinant **fowlpox** virus of claim 12, wherein the detectable marker is E. coli beta-glucuronidase.

15. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA encodes a cytokine.

16. The recombinant **fowlpox** virus of claim 15, wherein the cytokine is chicken myelomonocytic growth factor (cMGF) or chicken interferon (cIFN).

17. The recombinant **fowlpox** virus of claim 15, wherein the cytokine is selected from the group consisting of: interleukin-2, interleukin-6, interleukin-12, interferons, granulocyte-macrophage colony stimulating factors, and interleukin receptors.

18. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is under control of a promoter.

19. The recombinant **fowlpox** virus of claim 18, wherein the foreign DNA is under control of an endogenous upstream poxvirus promoter.

20. The recombinant **fowlpox** virus of claim 18, wherein the foreign DNA is under control of a heterologous upstream promoter.

21. The recombinant **fowlpox** virus of claim 18, wherein the promoter is a synthetic pox viral promoter.

22. The recombinant **fowlpox** virus of claim 21, wherein the synthetic pox viral promoter is selected from the group consisting of: pox synthetic late promoter 1, pox synthetic late promoter 2 early promoter 2, pox synthetic early promoter 1 late promoter 2, and pox synthetic early promoter 1.

23. A vaccine which comprises an effective immunizing amount of the recombinant **fowlpox** virus of claim 1 and a suitable carrier.

24. A method of immunizing an animal against an animal pathogen which comprises administering to the animal an effective immunizing dose of the vaccine of claim 23.

L3 ANSWER 5 OF 6 USPATFULL on STN
1998:108035 Self assembled, defective, nonself-propagating viral particles.
Mazzara, Gail P., Winchester, MA, United States
Panicali, Dennis L., Acton, MA, United States
Roberts, Bryan, Cambridge, MA, United States
Gritz, Linda R., Somerville, MA, United States
Stallard, Virginia, Seattle, WA, United States
Therion Biologics Corporation, Cambridge, MA, United States (U.S. corporation)
US 5804196 19980908
APPLICATION: US 1995-481031 19950607 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Recombinant avipox viral vectors which express heterologous polypeptides capable of assembling into defective nonself-propagating viral particles are disclosed. The recombinant avipox viruses can be used to produce significant amounts of the heterologous polypeptides in avian or non-avian cells. Preferably, the recombinant avipox virus is a fowlpox virus. The viral particles can also be used as immunogens and for targeted delivery of heterologous gene products and drugs.
CLM What is claimed is:
1. A pharmaceutical composition, comprising a self-assembled, defective nonself-propagating viral particle produced by a eukaryotic host cell transformed by a avipox virus vector, said avipox virus vector having inserted therein, at least two DNA sequences from a single species of lentivirus DNA sequences wherein one of the lentivirus DNA sequences is selected from the group consisting of the **gag** gene and **gag**-pol gene and portions thereof, such that the lentivirus DNA sequences express **gag**, **gag**-pol proteins, and portions thereof, referred to as said first lentivirus DNA sequence and a second lentivirus DNA sequence encoding another lentiviral protein, in the eukaryotic host cell infected with the pox virus vector, wherein the lentivirus proteins or portions thereof, self-assemble into defective, non-self-propagating lentivirus particles, in a pharmaceutically acceptable vehicle.

2. A method of delivery of a compound to a virally infected cell,

the pharmaceutical composition of claim 1.

3. A method of claim 2, wherein the virally infected cell is an RIV-infected, CD4 receptor-bearing cell and the viral particle comprises **HIV** core and envelope polypeptides.

4. The pharmaceutical composition of claim 1, wherein said second lentiviral DNA sequence is the env gene.

5. The pharmaceutical composition of claim 1, wherein the avipox is a **fowlpox** virus.

6. The pharmaceutical composition of claim 1, wherein the lentivirus is Simian Immunodeficiency Virus (SIV) or Human Immunodeficiency Virus (**HIV**).

L3 ANSWER 6 OF 6 USPATFULL on STN
97:42784 Self assembled, defective, non-self-propagating lentivirus particles.
Mazzara, Gail P., Winchester, MA, United States
Panicali, Dennis L., Acton, MA, United States
Roberts, Bryan, Cambridge, MA, United States
Gritz, Linda R., Somerville, MA, United States
Stallard, Virginia, Sequim, WA, United States
Mahr, Anna, Natick, MA, United States
Therion Biologics, Incorporated, Cambridge, MA, United States (U.S. corporation)
US 5631154 19970520
APPLICATION: US 1993-18344 19930216 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Recombinant avipox viral vectors which express heterologous polypeptides capable of assembling into defective nonself-propagating viral particles are disclosed. The recombinant avipox viruses can be used to produce significant amounts of the heterologous polypeptides in avian or non-avian cells. Preferably, the recombinant avipox virus is a fowlpox virus. The viral particles can also be used as immunogens and for targeted delivery of heterologous gene products and drugs.
CLM What is claimed:
1. An avipox virus vector having inserted therein at least two DNA sequences from a single species of lentivirus, wherein one of the lentivirus DNA sequences is the env gene and the other of the lentivirus DNA sequences is selected from the group consisting of the **gag** gene and **gag**-pol gene, such that the lentivirus DNA sequences express either env and **gag** proteins, or express env and **gag**-pol proteins in a eukaryotic host cell co-infected with the two pox virus vectors, and the lentivirus proteins self-assemble into defective, non-self-propagating lentivirus particles.

2. Two avipox virus vectors, each avipox virus vector having inserted therein only one of either of two DNA sequences from a single species of lentivirus, wherein one of the lentivirus DNA sequences is the env gene and the other of the lentivirus DNA sequences is selected from the group consisting of the **gag** gene and **gag**-pol gene, such that the lentivirus DNA sequences express either env and **gag** proteins, or express env and **gag**-pol proteins in a eukaryotic host cell co-infected with the two pox virus vectors, and the lentivirus proteins self-assemble into defective, non-self-propagating lentivirus particles.

3. The avipox vector of claim 1, wherein the avipox is a **fowlpox** virus.

4. The avipox vectors of claim 2, wherein each avipox is a **fowlpox** virus.

5. The avipox vector of claim 3, wherein the lentivirus is Simian Immunodeficiency Virus (SIV) or Human Immunodeficiency Virus (**HIV**).

6. The avipox vectors of claim 4, wherein the lentivirus particle is Simian Immunodeficiency Virus (SIV) or Human Immunodeficiency Virus (**HIV**).

7. A self-assembled, defective non-self-propagating lentivirus particle produced by eukaryotic host cell infected with the avipox virus vector of claim 1.

8. A self-assembled, defective non-self-propagating lentivirus particle produced by eukaryotic host cell infected with the avipox virus vector of claim 2.

9. The avipox vector of claim 5 wherein the lentivirus is **HIV**.

10. The avipox vector of claim 6 wherein the lentivirus is **HIV**.

11. A self-assembled, defective non-self-propagating lentivirus particle produced by eukaryotic host cell infected with the avipox virus vector of claim 9.

12. A self-assembled, defective non-self-propagating lentivirus particle produced by eukaryotic host cell infected with the avipox virus vector of claim 10.

=> d his

(FILE 'HOME' ENTERED AT 15:39:03 ON 06 MAR 2006)

FILE 'USPATFULL' ENTERED AT 15:39:18 ON 06 MAR 2006
L1 116 S (FOWLPOX/CLM OR TROVAC/CLM)
L2 53 S L1 AND AY<2000
L3 6 S L2 AND (HIV/CLM OR GAG/CLM)

=> s l1 and (TROVAC/clm)
12 TROVAC/CLM
L4 12 L1 AND (TROVAC/CLM)

=> d l14,cbib,ab,clm,1-12
L14 NOT FOUND
The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d l4,cbib,ab,clm,1-12

L4 ANSWER 1 OF 12 USPATFULL on STN
2005:292581 Recombinant vaccine against West Nile Virus.
Loosmore, Sheena May, Aurora, CANADA
Audonnet, Jean-Christophe Francis, Lyon, FRANCE
Minke, Jules Maarten, Corbas, FRANCE
US 2005255127 A1 20051117
APPLICATION: US 2003-714781 A1 20031117 (10)
PRIORITY: FR 2001-4737 20010406
US 2001-281923P 20010406 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An immunogenic or vaccine composition to induce an immune response or protective immune response against West Nile virus (WNV) in an animal susceptible to WNV. The composition includes a pharmaceutically or veterinarily acceptable vehicle or excipient, and a vector. The vector contains heterologous nucleic acid molecule(s), expresses in vivo in the animal WNV antigen, immunogen or epitope thereof, e.g., WNV E; WNV prM and E; WNV M and E; WNV prM, WNV M and E, WNV polyprotein prM-E, WNV polyprotein M-E, or WNV polyprotein prM-M-E. The composition can contain an adjuvant, such as carbomer. Methods for making and using such a composition, including prime-boost regimes and including as to differential diagnosis, are also contemplated.

CLM What is claimed is:

1. An immunogenic composition to induce an immune response against West Nile virus (WNV) in an animal susceptible to WNV comprising a vector comprising a recombinant virus or DNA plasmid that encodes and expresses in vivo in the animal WNV E; WNV prM and E; WNV M and E; WNV prM, WNV M and E, WNV polyprotein prM-E, WNV polyprotein M-E, or WNV polyprotein prM-M-E.

2. The immunogenic composition of claim 1 wherein the recombinant virus is a recombinant adenovirus, herpesvirus or poxvirus.

3. The immunogenic composition of claim 2 wherein the recombinant virus is a recombinant poxvirus.

4. The immunogenic composition of claim 3 wherein the recombinant poxvirus is a recombinant avipox virus.

5. The immunogenic composition of claim 4 wherein the recombinant avipox virus is a cannarypox or **fowlpox** virus.

6. The immunogenic composition of claim 5 wherein the canarypox virus is ALVAC and the **fowlpox** virus is **TROVAC**.

7. The immunogenic composition of claim 1 wherein the nucleic acid molecule is a coding frame encoding polyprotein prM-M-E.

8. The immunogenic composition of claim 5 wherein the nucleic acid molecule is a coding frame encoding polyprotein prM-M-E

molecule is a coding frame encoding polyprotein prM-M-E

10. The immunogenic composition of claim 1 wherein the nucleic acid molecule comprises nucleotides 466-741, 742-966 and 967-2469 of GenBank AF196835 encoding WNV prM, M and E, respectively.

11. The immunogenic composition of claim 1 wherein the nucleic acid molecule comprises nucleotides 466-2469 of GenBank AF196835 (SEQ ID NO: 66) encoding WN protein prM-M-E.

12. The immunogenic composition of claim 1 wherein the nucleic acid molecule comprises nucleotides 421-2469 of GenBank AF196835 (SEQ ID NO: 66) encoding WN protein prM-M-E and the signal peptide of prM.

13. The immunogenic composition of claim 1, further comprising an adjuvant.

14. The immunogenic composition according to claim 10, wherein the adjuvant is a carbomer.

15. The immunogenic composition of claim 1 further comprising an antigen or immunogen or epitope thereof of a pathogen other than WNV of the animal, or a vector that contains and expresses in vivo in the animal a nucleic acid molecule encoding the antigen, immunogen or epitope thereof, or an inactivated or attenuated pathogen other than WNV of the animal.

16. The immunogenic composition of claim 1, wherein the animal is a cat or a horse.

17. A method for inducing an immunological or protective immune response against WNV in an animal comprising administering to the animal the immunogenic or vaccine composition according to claim 1.

18. A method for inducing an immunological response against WNV in an animal comprising administering to the animal the immunogenic or vaccine composition according to claim 17.

19. The method according to claim 18 wherein the adjuvant comprises a carbomer adjuvant.

20. A method for inducing an immunological response against WNV in an animal and against another pathogen of the animal comprising administering to the animal the immunogenic composition according to 19.

21. A method for inducing an immunological response against WNV in an animal comprising administering to the animal (a) the immunogenic composition according to claim 1, and (b) a WNV isolated antigen, immunogen or epitope thereof, wherein (a) is administered prior to (b) in a prime-boost regimen, or (b) is administered prior to (a) in a prime-boost regimen, or (a) and (b) are administered together, either sequentially or in admixture.

22. The method of any of claims 17, 20 or 21, wherein the animal is a cat or a horse.

23. A differential diagnosis method comprising administering to animals an immunogenic composition of claim 1, and/or a WNV antigen, immunogen or epitope, and testing the animals for presence or absence of a WNV protein or antibody thereto not expressed by the immunogenic or vaccine composition or not administered as the WNV antigen, immunogen or epitope.

24. The method of claim 23, wherein the animal is a cat or a horse.

25. A kit for performing the method of claim 23 comprising (a) and (b) in separate containers, optionally with instructions for admixture and/or administration.

26. A kit for performing the method of claim 24 comprising the immunogenic composition and/or the WNV antigen, immunogen or epitope, and an assay for testing for the presence or absence of the WNV protein, in separate containers, optionally with instructions for administration of the immunogenic or vaccine composition and/or the WNV antigen, immunogen or epitope, and/or for performing the assay.

27. A kit comprising (a) the immunogenic composition according to claim 1, and (b) the antigen or immunogen or epitope thereof of a pathogen other than WNV of the animal, or the vector that contains and expresses in vivo in the animal a nucleic acid molecule encoding the antigen, immunogen or epitope thereof, or the inactivated or attenuated pathogen other than WNV of the animal, wherein (a) and (b) are in separate

and/or administration of (a) and (b).

28. The kit of claim 25 or 27, wherein the animal is a cat or a horse.

29. A plasmid that encodes and expresses in vivo in an animal susceptible to West Nile Virus WNV E; WNV prM and E; WNV M and E; WNV prM, WNV M and E, WNV polyprotein prM-E, WNV polyprotein M-E, or WNV polyprotein prM-M-E.

L4 ANSWER 2 OF 12 USPATFULL on STN
2005:130640 Tumor antigen BFA5 for prevention and / or treatment of cancer.
Berinstein, Neil, Toronto, CANADA
Gallichan, Scott, Campbellville, CANADA
Lovitt, Corey, Bolton, CANADA
Parrington, Mark, Bradford, CANADA
Pedyczak, Artur, Pickering, CANADA
Radvanyi, Laszlo, Richmond Hill, CANADA
Singh-Sandhu, Devender, Thornhill, CANADA
Aventis Pasteur, Ltd., Toronto, CANADA (non-U.S. corporation)
US 2005112099 A1 20050526
APPLICATION: US 2004-825026 A1 20040415 (10)
PRIORITY: US 2003-462945P 20030415 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a nucleic acid encoding a polypeptide and the use of the nucleic acid or polypeptide in preventing and/or treating cancer. In particular, the invention relates to improved vectors for the insertion and expression of foreign genes encoding tumor antigens for use in immunotherapeutic treatment of cancer.
CLM What is claimed is:
1. An expression vector comprising the nucleic acid sequence as illustrated in SEQ ID NO.: 5 or FIG. 4; a nucleic acid sequence encoding the amino acid sequence illustrated in SEQ ID NO.: 6 or FIG. 5; or a fragment thereof.

2. The expression vector of claim 1 wherein the vector is a plasmid or a viral vector.

3. The expression vector of claim 2 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

4. The expression vector of claim 3 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

5. The expression vector of claim 4 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

6. The expression vector of claim 1 further comprising at least one additional tumor-associated antigen.

7. The expression vector of claim 6 wherein the vector is a plasmid or a viral vector.

8. The expression vector of claim 7 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

9. The expression vector of claim 8 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

10. The expression vector of claim 9 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

11. The expression vector of claim 1 further comprising at least one nucleic sequence encoding an angiogenesis-associated antigen.

12. The expression vector of claim 1 wherein the vector is a plasmid or a viral vector.

13. The expression vector of claim 12 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

14. The expression vector of claim 13 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

15. The expression vector of claim 14 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

16. The expression vector of claim 6 further comprising at least one nucleic sequence encoding an angiogenesis-associated antigen.

17. The expression vector of claim 16 wherein the vector is a plasmid or a viral vector.

18. The expression vector of claim 17 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

19. The expression vector of claim 17 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

20. The expression vector of claim 18 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

21. An expression vector selected from the group consisting of an expression vector of claim 1, an expression vector of claim 6, an expression vector of claim 11, and an expression vector of claim 16; further comprising a nucleic acid sequence encoding a co-stimulatory molecule.

22. The expression vector of claim 22 wherein the vector is a plasmid or a viral vector.

23. The expression vector of claim 23 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

24. The expression vector of claim 24 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

25. The expression vector of claim 18 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

26. A composition comprising an expression vector in a pharmaceutically acceptable carrier, said vector comprising the nucleic acid sequence shown in SEQ ID NO.:5 or FIG. 4; a nucleic acid sequence encoding the amino acid sequence illustrated in SEQ ID NO.: 6 or FIG. 5; or a fragment thereof.

27. The composition of claim 26 wherein the vector is a plasmid or a viral vector.

28. The composition of claim 27 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

29. The composition of claim 28 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

30. The composition of claim 29 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

31. A method for preventing or treating cancer comprising administering to a host an expression vector comprising the nucleic acid sequence illustrated in SEQ ID NO.: 5 or FIG. 4; a nucleic acid encoding the amino acid sequence illustrated in SEQ ID NO.: 6 or FIG. 5; or a fragment thereof.

32. The method of claim 31 wherein the vector is a plasmid or a viral vector.

33. The method of claim 32 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

34. The method of claim 33 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

35. The method of claim 34 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

36. An isolated peptide derived from BFA5 as shown in Table X or XI.

37. A method for immunizing a host against the tumor antigen BFA5 comprising administering to the patient a peptide shown in Table X or XI, either alone or in combination with another agent, where the individual components of the combination are administered simultaneously or separately from one another.

38. An isolated peptide derived from BFA5 as shown in Table X or XI.

39. A method for immunizing a host against the tumor antigen BFA5 comprising administering to the patient a peptide shown in Table X or XI, either alone or in combination with another agent, where the individual components of the combination are administered simultaneously or separately from one another.

40. The expression vector of claim 6 wherein the additional tumor-associated antigen is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO.: 1; SEQ ID NO.: 3; the nucleic acid sequence shown in FIG. 1; the nucleic sequence illustrated in FIG. 3A; a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO.: 2; a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO.: 4; the nucleic acid sequence encoding the amino acid sequence illustrated in FIG. 2; a nucleic acid sequence encoding the amino acid sequence illustrated in FIG. 3B; a nucleic acid hybridizable under stringent conditions to any of the foregoing sequences; a fragment of any of the foregoing nucleic acid sequences; and, a derivative of any of the foregoing nucleic acid sequences.

41. The expression vector of claim 40 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

42. The expression vector of claim 41 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

43. The expression vector of claim 42 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

44. An expression vector selected from the group consisting of an expression vector of claim 40, an expression vector of claim 41, an expression vector of claim 42, and an expression vector of claim 42; further comprising a nucleic acid sequence encoding a co-stimulatory molecule.

45. An expression vector of claim 44 or claim 21 wherein the co-stimulatory molecule is human B7.1 or a derivative thereof.

46. A composition comprising an expression vector of claim 40 in a pharmaceutically acceptable carrier.

47. A composition comprising an expression vector of claim 41 in a pharmaceutically acceptable carrier.

48. A composition comprising an expression vector of claim 42 in a pharmaceutically acceptable carrier.

49. A composition comprising an expression vector of claim 43 in a pharmaceutically acceptable carrier.

50. A composition comprising an expression vector of claim 44 in a pharmaceutically acceptable carrier.

51. A composition comprising an expression vector of claim 45 in a pharmaceutically acceptable carrier.

52. A method for preventing or treating cancer comprising administering to a host a composition of claim 46.

53. A method for preventing or treating cancer comprising administering to a host a composition of claim 47.

54. A method for preventing or treating cancer comprising administering to a host a composition of claim 48.

55. A method for preventing or treating cancer comprising administering to a host a composition of claim 49.

56. A method for preventing or treating cancer comprising administering to a host a composition of claim 50.

57. A method for preventing or treating cancer comprising administering to a host a composition of claim 51.

58. An isolated DNA molecule comprising the nucleic acid of SEQ ID NO.:5 and at least one of the nucleic acid sequences of SEQ ID NO.: 3 or SEQ ID NO.: 5.

59. An expression vector comprising the isolated DNA molecule of claim 58.

60. An isolated DNA molecule comprising a nucleic acid encoding the amino acid sequence of SEQ ID NO. 6 and at least one of the amino acid sequences of SEQ ID NO.: 2 or SEQ ID NO.: 4.

61. An expression vector comprising the isolated DNA molecule of claim 60.

62. An isolated DNA molecule comprising the nucleic acid of SEQ ID NO.:5 and at least one of the nucleic acid sequences of SEQ ID NO.: 3 or SEQ ID NO.: 5; a nucleic acid hybridizable under stringent conditions to the nucleic acid sequences of SEQ ID NO.: 3 or SEQ ID NO.: 5; a fragment of the nucleic acid sequences of SEQ ID NO.: 3 or SEQ ID NO.: 5; and, a derivative of any of the nucleic acid sequences of SEQ ID NO.: 3 or SEQ ID NO.: 5.

63. An antibody having the ability to bind the amino acid sequence of SEQ ID NO.: 6 or a fragment the amino acid sequence of SEQ ID NO.: 6.

L4 ANSWER 3 OF 12 USPATFULL on STN
2005:36966 Recombinant vaccine against West Nile Virus.
Loosmore, Sheena May, Aurora, CANADA
Audonnet, Jean-Christophe Francis, Lyon, FRANCE
Minke, Jules Maarten, Corbas, FRANCE
Karaca, Kemal, Athens, GA, UNITED STATES
US 2005031641 A1 20050210
APPLICATION: US 2003-679520 A1 20031006 (10)
PRIORITY: FR 2001-4737 20010406
US 2001-281923P 20010406 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An immunogenic or vaccine composition to induce an immune response or protective immune response against West Nile virus (WNV) in an animal susceptible to WNV. The composition includes a pharmaceutically or veterinarily acceptable vehicle or excipient, and a vector. The vector contains heterologous nucleic acid molecule(s), expresses in vivo in the animal WNV antigen, immunogen or epitope thereof, e.g., WNV E; WNV prM and E; WNV M and E; WNV prM, WNV M and E, WNV polyprotein prM-E, WNV polyprotein M-E, or WNV polyprotein prM-M-E. The composition can contain an adjuvant, such as carbomer. Methods for making and using such a composition, including prime-boost regimes and including as to differential diagnosis, are also contemplated.
CLM What is claimed is:
1. An immunogenic composition to induce an immune response against West Nile virus (WNV) in an animal susceptible to WNV comprising a vector comprising a recombinant virus or DNA plasmid that encodes and expresses in vivo in the animal WNV E; WNV prM and E; WNV M and E; WNV prM, WNV M and E, WNV polyprotein prM-E, WNV polyprotein M-E, or WNV polyprotein prM-M-E.

2. The immunogenic composition of claim 1 wherein the recombinant virus is a recombinant adenovirus, herpesvirus or poxvirus.

3. The immunogenic composition of claim 2 wherein the recombinant virus is a recombinant poxvirus.

4. The immunogenic composition of claim 3 wherein the recombinant poxvirus is a recombinant avipox virus.

5. The immunogenic composition of claim 4 wherein the recombinant avipox virus is a cannarypox or **fowlpox** virus.

6. The immunogenic composition of claim 5 wherein the canarypox virus is ALVAC and the **fowlpox** virus is **TROVAC**.

7. The immunogenic composition of claim 1 wherein the nucleic acid molecule is a coding frame encoding polyprotein prM-M-E.

8. The immunogenic composition of claim 5 wherein the nucleic acid molecule is a coding frame encoding polyprotein prM-M-E

9. The immunogenic composition of claim 6 wherein the nucleic acid

10. The immunogenic composition of claim 1 wherein the nucleic acid molecule comprises nucleotides 466-741, 742-966 and 967-2469 of GenBank AF196835 encoding WNV prM, M and E, respectively.

11. The immunogenic composition of claim 1 wherein the nucleic acid molecule comprises nucleotides 466-2469 of GenBank AF196835 (SEQ ID NO: 66) encoding WN protein prM-M-E.

12. The immunogenic composition of claim 1 wherein the nucleic acid molecule comprises nucleotides 421-2469 of GenBank AF196835 (SEQ ID NO: 66) encoding WN protein prM-M-E and the signal peptide of prM.

13. The immunogenic composition of claim 1, further comprising an adjuvant.

14. The immunogenic composition according to claim 10, wherein the adjuvant is a carbomer.

15. The immunogenic composition of claim 1 further comprising an antigen or immunogen or epitope thereof of a pathogen other than WNV of the animal, or a vector that contains and expresses in vivo in the animal a nucleic acid molecule encoding the antigen, immunogen or epitope thereof, or an inactivated or attenuated pathogen other than WNV of the animal.

16. The immunogenic composition of claim 1, wherein the animal is a cat or a horse.

17. A method for inducing an immunological or protective immune response against WNV in an animal comprising administering to the animal the immunogenic or vaccine composition according to claim 1.

18. A method for inducing an immunological response against WNV in an animal comprising administering to the animal the immunogenic or vaccine composition according to claim 17.

19. The method according to claim 18 wherein the adjuvant comprises a carbomer adjuvant.

20. A method for inducing an immunological response against WNV in an animal and against another pathogen of the animal comprising administering to the animal the immunogenic composition according to 19.

21. A method for inducing an immunological response against WNV in an animal comprising administering to the animal (a) the immunogenic composition according to claim 1, and (b) a WNV isolated antigen, immunogen or epitope thereof, wherein (a) is administered prior to (b) in a prime-boost regimen, or (b) is administered prior to (a) in a prime-boost regimen, or (a) and (b) are administered together, either sequentially or in admixture.

22. The method of any of claims 17, 20 or 21, wherein the animal is a cat or a horse.

23. A differential diagnosis method comprising administering to animals an immunogenic composition of claim 1, and/or a WNV antigen, immunogen or epitope, and testing the animals for presence or absence of a WNV protein or antibody thereto not expressed by the immunogenic or vaccine composition or not administered as the WNV antigen, immunogen or epitope.

24. The method of claim 23, wherein the animal is a cat or a horse.

25. A kit for performing the method of claim 23 comprising (a) and (b) in separate containers, optionally with instructions for admixture and/or administration.

26. A kit for performing the method of claim 24 comprising the immunogenic composition and/or the WNV antigen, immunogen or epitope, and an assay for testing for the presence or absence of the WNV protein, in separate containers, optionally with instructions for administration of the immunogenic or vaccine composition and/or the WNV antigen, immunogen or epitope, and/or for performing the assay.

27. A kit comprising (a) the immunogenic composition according to claim 1, and (b) the antigen or immunogen or epitope thereof of a pathogen other than WNV of the animal, or the vector that contains and expresses in vivo in the animal a nucleic acid molecule encoding the antigen, immunogen or epitope thereof, or the inactivated or attenuated pathogen other than WNV of the animal, wherein (a) and (b) are in separate containers, and the kit optionally contains instructions for admixture

28. The kit of claim 25 or 27, wherein the animal is a cat or a horse.

29. A plasmid that encodes and expresses in vivo in an animal susceptible to West Nile Virus WNV E; WNV prM and E; WNV M and E; WNV prM, WNV M and E, WNV polyprotein prM-E, WNV polyprotein M-E, or WNV polyprotein prM-M-E.

L4 ANSWER 4 OF 12 USPATFULL on STN
2004:285789 Vaccines using high-dose cytokines.
Astsaturov, Igor, Baltimore, MD, UNITED STATES
Petrella, Teresa, North York, CANADA
DeBenedette, Mark, Toronto, CANADA
Berinstein, Neil, Toronto, CANADA
Spaner, David E., Toronto, CANADA
Sunnybrook and Women's College Health Sciences Center Aventis Pasteur, Ltd. (U.S. corporation)
US 2004223949 A1 20041111
APPLICATION: US 2003-690199 A1 20031021 (10)
PRIORITY: US 2002-420425P 20021022 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the field of cancer immunotherapy. In particular, vaccines are administered in conjunction with high doses of cytokines to enhance an anti-tumor immune response.
CLM What is claimed is:
1. A method for treating cancer comprising: a) administering to a host a composition containing a tumor antigen, fragment thereof or nucleic acid encoding the tumor antigen such that the host develops an immune response against the tumor antigen; and, b) subsequently administering to the host a high dose of a cytokine; whereby the combination of steps a) and b) provides an enhanced T cell response in the host relative to that which occurs following step a) alone.

2. The method of claim 1 wherein the tumor antigen is administered as a polypeptide or peptide.

3. The method of claim 1 wherein the composition comprises a nucleic acid encoding a tumor antigen.

4. The method of claim 3 wherein the nucleic acid is contained within a plasmid or a viral vector.

5. The method of claim 4 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

6. The method of claim 5 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, MVA, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

7. The method of claim 6 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

8. The method of claim 1 wherein the cytokine is IFN.

9. The method of claim 8 wherein the cytokine is IFN-α.

10. The method of claim 9 wherein the cytokine is IFN-α2b.

11. The method of claim 1 wherein the tumor antigen is selected from the group consisting of gp100, MART-1/Melan A, gp75/TRP-1, tyrosinase, NY-ESO-1, melanoma proteoglycan, a MAGE antigen, a BAGE antigen, a GAGE antigen, RAGE antigen, N-acetylglucosaminyltransferase-V, p15, β-catenin, MUM-1, cyclin dependent kinase-4, p21 -ras, BCR-abl, p53, p185 HER2/neu, epidermal growth factor receptor, carcinoembryonic antigen, modified carcinoembryonic antigen, carcinoma-associated mutated mucins, an Epstein Barr Virus EBNA gene product, papilloma virus E7, papilloma virus E6, prostate specific antigen, prostate specific membrane antigen, KSA, kinesin 2, HIP-55, TGFβ-1 anti-apoptotic factor, tumor protein D52, H1FT, an NY-BR antigen, fragments thereof, and derivatives thereof.

12. The method of claim 11 wherein the tumor antigen is selected from the group consisting of gp100, MAGE-1, MAGE-2, MAGE-3, MAGE-4, MAGE-6, MAGE-12, MAGE-51, GAGE-1, GAGE-2, RAGE-1, NY-BR-1, NY-BR-62, NY-BR-75, NY-BR-85, NY-BRP-87, and NY-BR-96.

13. The method of claim 12 wherein the tumor antigen is gp100.

vector encoding a tumor antigen or a fragment thereof and the cytokine is a T cell activating cytokine.

15. The method of claim 14 wherein poxviral vector is an ALVAC vector and the T cell activating cytokine is IFN.

16. The method of claim 15 wherein the T cell activating cytokine is IFNα.

17. The method of claim 16 wherein the T cell activating cytokine is IFNα2b.

18. The method of claim 17 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least two times per week for at least two weeks.

19. The method of claim 18 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least three times per week for at least two weeks.

20. The method of claim 19 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least four times per week for at least two weeks.

21. The method of claim 20 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least five times per week for at least two weeks.

22. The method of claim 21 wherein IFNα2b is administered at at least 20 MU/$m^{2/d}$ IV at least five times per week for at least four weeks.

L4 ANSWER 5 OF 12 USPATFULL on STN
2004:254386 Tumor antigens BFA4 and BCY1 for prevention and / or treatment of cancer.
Berinstein, Neil, Toronto, CANADA
Lovitt, Corey, Bolton, CANADA
Parrington, Mark, Bradford, CANADA
Pedyczak, Artur, Pickering, CANADA
Radvanyi, Laszlo, Richmond Hill, CANADA
Gallichan, Scott, Campbellville, CANADA
Singh-Sandhu, Devender, Thornhill, CANADA
Oomen, Raymond P., Aurora, CANADA
Cao, Shi-Xian, Stouffrille, CANADA
Aventis Pasteur, Ltd. (non-U.S. corporation)
US 2004197912 A1 20041007
APPLICATION: US 2003-611440 A1 20030701 (10)
PRIORITY: US 2002-394346P 20020703 (60)
US 2002-394503P 20020709 (60)
US 2002-411833P 20020918 (60)
US 2003-445342P 20030206 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a nucleic acid encoding a polypeptide and the use of the nucleic acid or polypeptide in preventing and/or treating cancer. In particular, the invention relates to improved vectors for the insertion and expression of foreign genes encoding tumor antigens for use in immunotherapeutic treatment of cancer.

CLM What is claimed is:

1. An expression vector comprising the nucleic acid sequence as illustrated in SEQ ID NO.: 1 or 3 or a fragment thereof.

2. The expression vector of claim 1 wherein the vector is a plasmid or a viral vector.

3. The expression vector of claim 2 wherein the viral vector is selected from the group consisting of poxvirus, alphavirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

4. The expression vector of claim 3 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

5. The expression vector of claim 4 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

6. The expression vector of claim 1 further comprising at least one additional tumor-associated antigen.

viral vector.

8. The expression vector of claim 7 wherein the viral vector is selected from the group consisting of poxvirus, alphavirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

9. The expression vector of claim 8 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

10. The expression vector of claim 9 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

11. The expression vector of claim 1 further comprising at least one nucleic sequence encoding an angiogenesis-associated antigen.

12. The expression vector of claim 11 wherein the vector is a plasmid or a viral vector.

13. The expression vector of claim 12 wherein the viral vector is selected from the group consisting of poxvirus, alphavirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

14. The expression vector of claim 13 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

15. The expression vector of claim 14 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

16. The expression vector of claim 6 further comprising at least one nucleic sequence encoding an angiogenesis-associated antigen.

17. The expression vector of claim 16 wherein the vector is a plasmid or a viral vector.

18. The expression vector of claim 17 wherein the viral vector is selected from the group consisting of poxvirus, alphavirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

19. The expression vector of claim 17 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

20. The poxvirus of claim 18 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

21. The expression vector of claim 1, 6, 11 or 16 further comprising at least one nucleic acid sequence encoding a co-stimulatory component.

22. The expression vector of claim 22 wherein the vector is a plasmid or a viral vector.

23. The expression vector of claim 23 wherein the viral vector is selected from the group consisting of poxvirus, alphavirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

24. The expression vector of claim 24 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

25. The poxvirus of claim 18 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

26. A composition comprising an expression vector in a pharmaceutically acceptable carrier, said vector comprising the nucleic acid sequence shown in SEQ ID NO.: 1 or 3 or a fragment thereof.

27. The expression vector of claim 26 wherein the vector is a plasmid or a viral vector.

28. The expression vector of claim 27 wherein the viral vector is selected from the group consisting of poxvirus, alphavirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

29. The expression vector of claim 28 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

30. The poxvirus of claim 29 wherein the viral vector is a poxvirus

31. A method for preventing or treating cancer comprising administering to a host an expression vector comprising the nucleic acid sequence illustrated in SEQ ID NO.: 1 or 3 or a fragment thereof.

32. The expression vector of claim 31 wherein the vector is a plasmid or a viral vector.

33. The expression vector of claim 32 wherein the viral vector is selected from the group consisting of poxvirus, alphavirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

34. The expression vector of claim 33 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

35. The poxvirus of claim 34 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

36. A peptide derived from BFA4 as shown in Table V, VI or VII.

37. A method for immunizing a host against the tumor antigen BFA4 comprising administering to the patient a peptide shown in Table V, VI or VII, either alone or in combination with another agent, where the individual components of the combination are administered simultaneously or separately from one another.

38. A peptide derived from BCY1 as shown in Table VIII or IX.

39. A method for immunizing a host against the tumor antigen BCY1 comprising administering to the patient a peptide shown in Table VIII or IX, either alone or in combination with at least one other agent, where the individual components of the combination are administered simultaneously or separately from one another.

L4 ANSWER 6 OF 12 USPATFULL on STN
2004:44244 Immunogenic polypetides encoded by mage minigenes and uses thereof.
Berinstein, Neil, Toronto, CANADA
Tartaglia, James, Aurora, CANADA
Tine, John A., Scotia, NY, UNITED STATES
Moingeon, Philippe, Pommiers, FRANCE
Boon-Falleur, Thierry, Brussels, BELGIUM
Vander Bruggen, Pierre, Brussels, BELGIUM
US 2004033234 A1 20040219
APPLICATION: US 2003-275993 A1 20030708 (10)
WO 2001-CA646 20010507
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention discloses immunogenic polypeptides comprising several MAGE-specific antigen epitopes selected from different (i.e. discrete) members of the MAGE protein family, nucleic acids coding therefor, recombinant viruses and/or cells comprising said nucleic acids, and compositions thereof. Methods for eliciting or inducing MAGE-specific immune responses utilizing the aforementioned immunogenic agents are also disclosed.
CLM What is claimed is:
1. An immunogenic polypeptide comprising a first MAGE-specific antigen epitope of a member selected from the group consisting of MAGE 1, MAGE 2 and MAGE 3, and a second MAGE-specific antigen epitope of a different member selected from said group.

2. The polypeptide of claim 1 wherein the first MAGE-specific antigen epitope is from MAGE 1 and the second MAGE-specific antigen epitope is from MAGE 3.

3. The polypeptide of claim 2 wherein the epitope from MAGE 1 has the sequence EADPTGHSY and the epitope of MAGE 3 has the sequence EVDPIGHLY.

4. The polypeptide of claim 1 wherein the first MAGE-specific antigen epitope and the second MAGE-specific antigen epitope are adjoined together.

5. The polypeptide of claim 1 wherein an amino acid linker sequence joins the first and second MAGE-specific antigen epitope.

6. The polypeptide of claim 5 wherein the linker amino acid sequence further comprises a protease cleavage site.

7. The polypeptide of claim 1 comprising the amino acid sequence of SEQ. ID NO:1.

NO.:1.

9. A pharmaceutical composition comprising the polypeptide of any one of claim 1 through 8, and a pharmaceutically acceptable diluent or carrier.

10. The composition of claim 9 further comprising an adjuvant.

11. A nucleic acid comprising a nucleic acid sequence which encodes the polypeptide of any one of claims 1 through 8.

12. The nucleic acid of claim 11 which encodes the polypeptide of claim 7.

13. The nucleic acid of claim 11 wherein the sequence which encodes the polypeptide has the sequence of SEQ. ID NO:2.

14. The nucleic acid of any one of claims 11 through 13 wherein the nucleic acid is selected from the group consisting of viral nucleic acid, plasmids, bacterial DNA, naked/free DNA, and RNA.

15. The viral nucleic acid of claim 14 wherein the virus is selected from the group consisting of adenovirus, alphavirus, and poxvirus.

16. The poxvirus of claim 15 selected from the group consisting of vaccinia, **fowlpox**, and avipox.

17. The poxvirus of claim 15 selected from the group consisting of **TROVAC**, ALVAC, NYVAC, and MVA.

18. The poxvirus of claim 15 wherein the poxvirus is ALVAC.

19. A pharmaceutical composition comprising the nucleic acid of any one of claim 11 through 18, and a pharmaceutically acceptable diluent or carrier.

20. The pharmaceutical composition of claim 19 further comprising an adjuvant.

21. A cell comprising a nucleic acid according to any one of claims 11 through 18 wherein the cell expresses the polypeptide.

22. The cell of claim 21 wherein the cell binds cleavage fragments of the polypeptide.

23. The cell of claim 22 wherein the cleavage fragments are produced by a protease.

24. The cell of claim 21 wherein the cell additionally expresses a MHC HLA class 1 molecule.

25. The cell of claim 21 wherein the cell is an antigen-presenting cell.

26. The cell of claim 25 wherein the cell is a dendritic cell.

27. A recombinant virus comprising a virus into which is inserted a nucleic acid encoding for a polypeptide of any one of claim 1 through 8, the recombinant virus causing the expression of the polypeptide in an infected cell.

28. A recombinant virus into which is inserted a nucleic acid coding for a polypeptide according to any one of claims 1 through 8, wherein cells infected with said recombinant virus are capable of eliciting an immune response directed against a member selected from the group consisting of: the polypeptide; a MAGE-specific antigen epitope of the polypeptide; a MAGE protein or fragment thereof comprising a MAGE-specific antigen epitope of the polypeptide; cells expressing MAGE protein or fragments thereof, the polypeptide, a MAGE-specific antigen epitope of the polypeptide; and cells binding said MAGE protein or fragments thereof, the polypeptide, a MAGE-specific antigen epitope of the polypeptide.

29. The recombinant virus of claim 28 selected from the group consisting of adenovirus, alphavirus and poxvirus.

30. The recombinant virus of either one of claim 27 or 28 wherein the virus is ALVAC.

31. A pharmaceutical composition comprising the recombinant virus of any one of claims 27 through 30 and a pharmaceutically acceptable diluent or carrier.

32. The composition of claim 31 further comprising an adjuvant.

33. A method of inducing an immune response in an animal directed against a member selected from the group consisting of: a polypeptide as claimed in any one of claim 1 through 8, a MAGE-specific antigen epitope of said polypeptide, a MAGE protein or fragment thereof comprising a MAGE-specific antigen epitope of said polypeptide, cells expressing said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, and cells binding said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, comprising administering to said animal a recombinant virus according to any one of claims 27 through 30 in an amount sufficient to induce an immune response.

34. A method of inducing an immune response in an animal directed against a member selected from the group consisting of: a polypeptide as claimed in any one of claims 1 through 8, a MAGE-specific antigen epitope of said polypeptide, a MAGE protein or fragment thereof comprising a MAGE-specific antigen epitope of said polypeptide, cells expressing said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, and cells binding said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, comprising administering to said animal a nucleic acid according to any one of claims 11 through 18 in an amount sufficient to induce an immune response.

35. A method of inducing an immune response in an animal directed against a member selected from the group consisting of: a polypeptide as claimed in any one of claims 1 through 8, a MAGE-specific antigen epitope of said polypeptide, a MAGE protein or fragment thereof comprising a MAGE-specific antigen epitope of said polypeptide, cells expressing said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, and cells binding said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, comprising administering to said animal a polypeptide according to any one of claims 1 though 8 in an amount sufficient to induce an immune response.

36. A method of inducing an immune response in an animal directed against a member selected from the group consisting of: a polypeptide as claimed in any one of claims 1 through 8, a MAGE-specific antigen epitope of said polypeptide, a MAGE protein or fragment thereof comprising a MAGE-specific antigen epitope of said polypeptide, cells expressing said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, and cells binding said MAGE protein or fragment thereof, polypeptide, MAGE-specific antigen epitope of the polypeptide, comprising administering to said animal a cell according to any one of claims 21 through 26 in an amount sufficient to induce an immune response.

37. A treatment for cancer comprising any one of the methods of claims 33 through 36.

38. The use of an immunogenic polypeptide of claim 1 for the manufacture of a medicament for the treatment of cancer.

39. The use of claim 38 wherein said polypeptide comprises the amino acid sequence of SEQ. ID NO:1.

40. The use of an isolated, purified or recombinant nucleic acid sequence having the sequence of SEQ. ID NO:2 for the manufacture of a medicament for the treatment of cancer.

L4 ANSWER 7 OF 12 USPATFULL on STN
2004:12667 Enhancing the immune response to an antigen by presensitzing with an inducing agent prior to immunizing with the agent and the antigen.
Emtage, Peter, Boston, MA, UNITED STATES
Barber, Brian H., Mississauga, CA, UNITED STATES
Sambhara, Suryprakash, Decatur, GA, UNITED STATES
Sia, Charles Dwo Yuan, Toronto, CANADA
US 2004009185 A1 20040115
APPLICATION: US 2003-168417 A1 20030520 (10)
WO 2001-CA5 20010105
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of enhancing an immune response is disclosed. Th method involves an initial priming of the animal with an inducing agent, subsequently followed by administration of an inducing agent-antigen mixture. The antigen may be a tumour associated antigen, pathogenic organism antigen, autoimmune antigen, immunogenic fragment thereof, or a nucleic acid coding therefor.
CLM What is claimed is:
1. A method of enhancing an immune response to an antigen in an animal

the animal followed by (b) administering an effective amount of the inducing agent and the antigen to the animal.

2. A method according to claim 1 wherein the inducing agent is a bacterial toxoid.

3. A method according to claim 2 wherein the bacterial toxoid is tetanus toxoid or diphtheria toxoid.

4. A method according to any one of claims 1 to 3 wherein the antigen is a protein.

5. A method according to claim 4 wherein the antigen is selected from the group consisting of tumor antigens, autoimmune antigens and an antigen isolated from a pathogenic organism.

6. A method according to claim 5 wherein the tumor antigen is selected from the group consisting of gp100, carcinoembryonic antigen, tyrosinase, TRP-1, TRP-2, MART-1/Melan A, MAGE family, BAGE family, GAGE family, RAGE family, KSA, NY ESO-1, MUC-1, MUC-2, p53, p185, HER2/neu, PSA and PSMA and modified forms thereof.

7. A method according to claim 5 wherein the tumor antigen is gp100 or carcinoembryonic antigen or a modified form thereof.

8. A method according to claim 7 wherein the antigen is GP100 or modified gp100 having the sequence as shown in FIG. 2 (SEQ.ID.NO.:2).

9. A method according to claim 7 wherein the antigen is carcinoembryonic antigen (CEA) or modified CEA having the sequence shown in FIG. 3 (SEQ.ID.NO.:4).

10. A method according to any one of claims 1-9 wherein the antigen is administered as a nucleic acid sequence encoding the antigen.

11. A method according to claim 10 wherein the nucleic acid sequence is in a vector, plasmid or bacterial DNA.

12. A method according to claim 11 wherein the vector is a viral vector.

13. A method according to claim 12 wherein the viral vector is selected from adenovirus, alphavirus, and poxvirus.

14. A method according to claim 13 wherein the poxvirus is selected from the group consisting of vaccinia, **fowlpox** and avipox.

15. A method of claim 14 wherein the poxvirus is selected from the group comprising **TROVAC**, ALVAC, NYVAC, and MVA.

16. A method according to any one of claims 1 to 15 wherein step (b) occurs from about 3 weeks to about 6 weeks after step (a).

17. A method according to any one of claims 1 to 15 wherein step (b) occurs from about 3 weeks to about 4 weeks after step (a).

18. A method according to any one of claims 1 to 17 further comprising (c) administering a second dose of the inducing agent and the antigen.

19. A method according to claim 18 wherein step (c) occurs from about 3 weeks to about 6 we ks after step (b).

20. A method according to claim 18 wherein step (c) occurs from about 3 weeks to about 4 weeks after step (b).

21. A method according to any one of claims 1-20 wherein the antigen is administered in combination with at least one member selected from the group consisting of cytokines, lymphokines, co-stimulatory molecules, and nucleic acids coding therefor.

22. A method according to any one of claims 1-21 wherein the antigen is administered in combination with an adjuvant.

23. A method according to any one of claims 1-22 wherein the inducing agent is tetanus toxoid or diphtheria toxoid and the antigen is a tumor antigen.

24. A method according to claim 23 for the treatment of cancer.

25. A vaccine composition comprising an inducing agent and an antigen.

26. A use of a vaccine composition according to claim 25 to enhanc an immune response.

L4 ANSWER 8 OF 12 USPATFULL on STN
2003:214330 MAGE-A1 peptides for treating or preventing cancer.
Emtage, Peter, Boston, MA, UNITED STATES
Karunakaran, Liza, Toronto, CANADA
Pedyczak, Arthur, Toronto, CANADA
Barber, Brian H., Hawthorne, NY, UNITED STATES
US 2003148973 A1 20030807
APPLICATION: US 2002-150797 A1 20020517 (10)
PRIORITY: US 2001-292590P 20010523 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a nucleic acid encoding a polypeptide and the use of the nucleic acid or polypeptide in preventing and/or treating cancer. In particular, the invention relates to improved vectors for the insertion and expression of foreign genes encoding tumor antigens for use in immunotherapeutic treatment of cancer.

CLM What is claimed is:

1. An immunogenic peptide selected from the group consisting of SEQ ID NO.:1, SEQ ID NO.:2, SEQ ID NO.:3, and SEQ ID NO.:4.

2. An immunogenic composition comprising a peptide of claim 1 in a pharmaceutically acceptable carrier.

3. An immunogenic polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO.:1, SEQ ID NO.:2, SEQ ID NO.:3, and SEQ ID NO.:4.

4. An immunogenic composition comprising a polypeptide of claim 3 in a pharmaceutically acceptable carrier.

5. An isolated nucleic acid encoding an immunogenic peptide selected from the group consisting of SEQ ID NO.:1, SEQ ID NO.:2, SEQ ID NO.:3, and SEQ ID NO.:4.

6. A composition comprising a nucleic acid of claim 5 in a pharmaceutically acceptable carrier.

7. An isolated nucleic acid encoding an immunogenic peptide selected from the group consisting of:

AAAGTCCTTGAGTATGTGATCAAGGTC; (SEQ.ID.NO.28)

TTGCAGCTGGTCTTTGGCATTGACGTG; (SEQ.ID.NO.29)

AGTGCCTATGGGGAGCCCAGGAAGCTG; and, (SEQ.ID.NO.30)

TGCCTAGGTCTCTCCTATGATGGCCTG. (SEQ.ID.NO.31)

8. A composition comprising a nucleic acid of claim 7 in a pharmaceutically acceptable carrier.

9. An expression vector comprising a nucleic acid sequence encoding an immunogenic peptide selected from the group consisting of SEQ ID NO.: 1, SEQ ID NO.:2, SEQ ID NO.:3, and SEQ ID NO.:4.

10. The expression vector of claim 9 wherein the vector is a plasmid or a viral vector.

11. The expression vector of claim 10 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

12. The expression vector of claim 11 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

13. The expression vector of claim 12 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

14. An expression vector comprising a nucleic acid sequence encoding an immunogenic peptide selected from the group consisting of:

AAAGTCCTTGAGTATGTGATCAAGGTC; (SEQ.ID.NO.28)

TTGCAGCTGGTCTTTGGCATTGACGTG; (SEQ.ID.NO.29)

AGTGCCTATGGGGAGCCCAGGAAGCTG; and, (SEQ.ID.NO.30)

TGCCTAGGTCTCTCCTATGATGGCCTG. (SEQ.ID.NO.31)

a viral vector.

16. The expression vector of claim 15 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

17. The expression vector of claim 16 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

18. The expression vector of claim 17 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

19. A composition comprising an expression vector of claim 7 or 14 in a pharmaceutically acceptable carrier.

20. A method for preventing or treating cancer comprising administering to a host a peptide of claim 1.

21. A method for preventing or treating cancer comprising administering to a host a polypeptide of claim 3.

22. A method for preventing or treating cancer comprising administering to a host an expression vector of claim 7.

23. A method for preventing or treating cancer comprising administering to a host an expression of claim 14.

24. A host cell comprising a peptide selected from the group consisting of SEQ ID NO.:1, SEQ ID NO.:2, SEQ ID NO.:3, and SEQ ID NO.:4.

25. A method for preventing or treating cancer comprising administering to a patient a host cell of claim 23.

26. A method for inducing an immune response in a patient comprising: a) obtaining autologous cells from said patient; b) pulsing said cells in vitro with a peptide selected from the group consisting of SEQ ID NO.:1, SEQ ID NO.:2, SEQ ID NO.:3, and SEQ ID NO.:4; and, c) administering the cells of step b to said patient.

27. A method for inducing an immune response in a patient comprising: a) obtaining autologous cells from said patient; b) transfecting said cells in vitro with a nucleic acid encoding a peptide selected from the group consisting of SEQ ID NO.: 1, SEQ ID NO.:2, SEQ ID NO.:3, and SEQ ID NO.:4; and, c) administering the cells of step b to said patient.

L4 ANSWER 9 OF 12 USPATFULL on STN
2003:166063 Immunogenic targets for melanoma.
Emtage, Peter, Sunnyvale, CA, UNITED STATES
Karunakaran, Liza, Thornhill, CANADA
Pedyczak, Artur, Pickering, CANADA
Barber, Brian, White Plains, NY, UNITED STATES
Aventis Pasteur, Ltd. (U.S. corporation)
US 2003113919 A1 20030619
APPLICATION: US 2002-219850 A1 20020815 (10)
PRIORITY: US 2001-313438P 20010817 (60)
US 2001-313572P 20010817 (60)
US 2001-313573P 20010817 (60)
US 2001-313574P 20010817 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to peptides, polypeptides, and nucleic acids and the use of the peptide, polypeptide or nucleic acid in preventing and/or treating cancer. In particular, the invention relates to peptides and nucleic acid sequences encoding such peptides for use in diagnosing, treating, or preventing melanoma.
CLM What is claimed:
1. An expression vector comprising at least one nucleic acid sequence selected from the group consisting of 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48,49, 50, 51, 52, and 53.

2. The expression vector of claim 1 wherein the vector is a plasmid or a viral vector.

3. The expression vector of claim 2 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

4. The expression vector of claim 3 wherein the viral vector is a

canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

5. The expression vector of claim 4 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

6. The expression vector of claim 1 further comprising at least one additional tumor-associated antigen.

7. The expression vector of claim 6 wherein the vector is a plasmid or a viral vector.

8. The expression vector of claim 7 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

9. The expression vector of claim 8 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

10. The expression vector of claim 9 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

11. The expression vector of claim 1 further comprising at least one nucleic sequence encoding an angiogenesis-associated antigen.

12. The expression vector of claim 11 wherein the vector is a plasmid or a viral vector.

13. The expression vector of claim 12 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

14. The expression vector of claim 13 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

15. The expression vector of claim 14 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

16. The expression vector of claim 6 further comprising at least one nucleic sequence encoding an angiogenesis-associated antigen.

17. The expression vector of claim 16 wherein the vector is a plasmid or a viral vector.

18. The expression vector of claim 17 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

19. The expression vector of claim 17 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

20. The poxvirus of claim 18 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

21. The expression vector of claim 1, 6, 11 or 16 further comprising at least one nucleic acid sequence encoding a co-stimulatory component.

22. The expression vector of claim 22 wherein the vector is a plasmid or a viral vector.

23. The expression vector of claim 23 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

24. The expression vector of claim 24 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

25. The poxvirus of claim 18 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

26. A composition comprising an expression vector in a pharmaceutically acceptable carrier, said vector comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, and 53.

a viral vector.

28. The expression vector of claim 27 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

29. The expression vector of claim 28 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

30. The poxvirus of claim 29 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

31. A method for preventing or treating cancer comprising administering to a host an expression vector comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, and 53.

32. The expression vector of claim 31 wherein the vector is a plasmid or a viral vector.

33. The expression vector of claim 32 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

34. The expression vector of claim 33 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

35. The poxvirus of claim 34 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

36. A peptide selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, and 26.

37. A composition comprising peptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, and 26 in a pharmaceutically acceptable carrier.

38. A method for preventing or treating cancer comprising administering to a peptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, and 26.

L4 ANSWER 10 OF 12 USPATFULL on STN
1999:43194 Infectious bursal disease virus recombination poxvirus vaccine.
Paoletti, Enzo, Delmar, NY, United States
Taylor, Jill, Albany, NY, United States
Gettig, Russell, Averill Park, NY, United States
Virogenetics Corporation, Troy, NY, United States (U.S. corporation)
US 5891442 19990406
APPLICATION: US 1995-480697 19950607 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB What is described is a recombinant poxvirus, such as fowlpox virus, containing foreign DNA from infectious bursal disease virus. What is also described is a vaccine containing the recombinant poxvirus for inducing an immunological response in a host animal inoculated with the vaccine.
CLM What is claimed is:
1. A recombinant avipox virus comprising DNA from infectious bursal disease virus which codes for and is expressed as an infectious bursal disease virus structural protein VP2 or polyprotein VP2, VP3, VP4, wherein the recombinant avipox virus induces an immunological response in a host animal inoculated therewith.

2. A **TROVAC** recombinant poxvirus or a poxvirus having all of the identifying characteristics of **TROVAC** comprising exogenous DNA from infectious bursal disease virus.

3. The recombinant avipox virus of claim 1 which is a **fowlpox** virus.

4. The recombinant avipox virus of claim 3 which is a **TROVAC fowlpox** virus or a poxvirus having all of the identifying characteristics of **TROVAC**.

5. The recombinant avipox virus of claim 4 wherein the DNA from infectious bursal disease virus codes for and is expressed as infectious

6. The recombinant avipox virus of claim 4 which is vFP115 or vFP116.

7. The recombinant avipox virus of claim 1 which is a **fowlpox** virus which has attenuated virulence through approximately 50 serial passages on chicken embryo firbroblast cells, then subjecting the **fowlpox** virus to four successive plaque purifications, and obtaining a plaque isolate and further amplifying the isolate in primary chick embryo fibroblast cells.

8. The recombinant avipox virus of claim 4 wherein the DNA from infectious bursal disease virus codes for and is expressed as infectious bursal disease virus structural polyprotein VP2, VP3, VP4.

9. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 1.

10. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 2.

11. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 3.

12. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 5.

13. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 4.

14. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 6.

15. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 7.

16. An immunological composition for inducing an immunological response in a host inoculated with the immunological composition, said immmunological composition comprising a carrier and the recombinant avipox virus of claim 8.

17. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 9.

18. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 10.

19. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 11.

20. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 12.

21. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 13.

22. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 14.

23. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 15.

24. A method for inducing an immunological response in a host comprising administering to the host the immunological composition of claim 16.

25. The method of claim 17 wherein the host is a chicken.

26. The method of claim 18 wherein the host is a chicken.

28. The method of claim 20 wherein the host is a chicken.

29. The method of claim 21 wherein the host is a chicken.

30. The method of claim 22 wherein the host is a chicken.

31. The method of claim 23 wherein the host is a chicken.

32. The method of claim 24 wherein the host is a chicken.

33. A method for preparing an infectious bursal disease virus structural protein comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 1 and culturing the cells under conditions allowing expression of the infectious bursal disease virus structural protein by the avipox virus.

34. A method for preparing an infectious bursal disease virus gene product comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 2 and culturing the cells under conditions allowing expression of the infectious bursal disease virus gene product by the avipox virus.

35. A method for preparing an infectious bursal disease virus structural protein comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 3 and culturing the cells under conditions allowing expression of the infectious bursal disease virus structural protein by the avipox virus.

36. A method for preparing an infectious bursal disease virus structural protein comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 5 and culturing the cells under conditions allowing expression of the infectious bursal disease virus structural protein by the avipox virus.

37. A method for preparing an infectious bursal disease virus structural protein comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 4 and culturing the cells under conditions allowing expression of the infectious bursal disease virus structural protein by the avipox virus.

38. A method for preparing an infectious bursal disease virus structural protein comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 6 and culturing the cells under conditions allowing expression of the infectious bursal disease virus structural protein by the avipox virus.

39. A method for preparing an infectious bursal disease virus structural protein comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 7 and culturing the cells under conditions allowing expression of the infectious bursal disease virus structural protein by the avipox virus.

40. A method for preparing an infectious bursal disease virus structural protein comprising introducing into cells of an in vitro cell culture a recombinant avipox virus of claim 8 and culturing the cells under conditions allowing expression of the infectious bursal disease virus structural protein by the avipox virus.

L4 ANSWER 11 OF 12 USPATFULL on STN
1998:68530 Trova fowl pox virus recombinants comprising heterologous inserts.
Paoletti, Enzo, Delmar, NY, United States
Perkus, Marion E., Altamont, NY, United States
Taylor, Jill, Albany, NY, United States
Tartaglia, James, Schenectady, NY, United States
Norton, Elizabeth K., Latham, NY, United States
Riviere, Michel, Ecully, France
de Taisne, Charles, Lyons, France
Limbach, Keith J., Troy, NY, United States
Johnson, Gerard P., Waterford, NY, United States
Pincus, Steven E., East Greenbush, NY, United States
Cox, William I., Troy, NY, United States
Audonnet, Jean-Christophe Francis, Albany, NY, United States
Gettig, Russell Robert, Averill Park, NY, United States
Virogenetics Corporation, Troy, NY, United States (U.S. corporation)
US 5766599 19980616
APPLICATION: US 1995-458101 19950601 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB What is described is a modified vector, such as a recombinant poxvirus, particularly recombinant vaccinia virus, having enhanced safety. The

functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open reading frame encoding a virulence factor. In another embodiment, the genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus vaccines.

CLM What is claimed is:

1. An attenuated virus having all the identifying characteristics of: a **TROVAC fowlpox** virus.

2. A virus which is **TROVAC**.

3. A vector which comprises the virus of claim 1.

4. A vector which comprises the virus of claim 2.

5. A virus as claimed in claim 2 further comprising exogenous DNA from a non-poxvirus source in a nonessential region of the virus genome.

6. A virus as claimed in claim 5 wherein the exogenous DNA is selected from the group consisting of rabies virus, Hepatitis B virus, Japanese encephalitis virus, yellow fever virus, Dengue virus, measles virus, pseudorabies virus, Epstein-Barr virus, herpes simplex virus, human immunodeficiency virus, simian immunodeficiency virus, equine herpes virus, bovine herpes virus, bovine viral diarrhea virus, human cytomegalovirus, canine parvovirus, equine influenza virus, feline leukemia virus, feline herpes virus, Hantaan virus, C. tetani, avian influenza virus, mumps virus and Newcastle Disease virus.

7. A virus as claimed in claim 6 wherein the non-poxvirus source is avian influenza virus and the **fowlpox** virus is vFP89, vFP92, vFP100 or vFP122.

8. A virus as claimed in claim 6 wherein the virus is a **fowlpox** virus, the non-poxvirus source is human immunodeficiency virus and the **fowlpox** virus is vFP62, vFP63 or vFP174.

9. A virus as claimed in claim 6 wherein the non-poxvirus source is Newcastle Disease virus and the **fowlpox** virus is vFP96.

10. A virus as claimed in claim 6 which is a human immunodeficiency virus recombinant **fowlpox** virus which is vFP62 or vFP63.

11. A virus as claimed in claim 1 further comprising exogenous DNA from a non-poxvirus source in a nonessential region of the virus genome.

12. An immunological composition for inducing an immunological response in a host animal inoculated with said composition, said composition comprising the virus of any one of claims 1, 2 or 10 or 11, or, a vector as claimed in claim 3 or 4, and a carrier.

13. The immunological composition of claim 12 containing the virus or vector in an amount sufficient to induce a protective immunological response such that the immunological composition is a vaccine.

14. A method of expressing a gene product in a cell cultured in vitro comprising introducing into the cell a virus as claimed in any one of claims 1, 2 or 10 or 11, or, a vector as claimed in claim 3 or 4, transforming cell with the expression vector, cultivating the transformed cell under conditions which allow expression of the gene product, and further purifying the product.

L4 ANSWER 12 OF 12 USPATFULL on STN

1998:61172 Marek's disease virus recombinant poxvirus vaccine.

Paoletti, Enzo, Delmar, NY, United States
Taylor, Jill, Albany, NY, United States
Tartaglia, James, Schenectady, NY, United States
Ross, Louis, Alconbury, United Kingdom
Virogenetics Corporation, Troy, NY, United States (U.S. corporation)

US 5759552 19980602
APPLICATION: US 1994-207792 19940307 (8)
DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB What is described is a recombinant poxvirus, such as vaccinia virus or fowlpox virus, containing foreign DNA from Marek's disease virus. What is also described is a vaccine containing the recombinant poxvirus for inducing an immunological response in a host animal inoculated with the vaccine.

1. A recombinant **TROVAC fowlpox** comprising exogenous DNA encoding at least one of Marek's Disease Virus gB and gD glycoproteins.

2. The recombinant **TROVAC fowlpox** virus of claim 1 comprising exogenous DNA encoding Marek's Disease Virus gB glycoprotein.

3. The recombinant **TROVAC fowlpox** virus of claim 1 comprising exogenous DNA encoding Marek's Disease Virus gD glycoprotein.

4. The recombinant **TROVAC fowlpox** virus of claim 1 comprising exogenous DNA encoding Marek's Disease Virus gB and gD glycoproteins.

5. The recombinant **TROVAC fowlpox** virus of claim 1 comprising vFP108.

6. An immunological composition comprising a carrier and a recombinant **TROVAC fowlpox** virus as claimed in any one of claims 1 to 5.

7. The immunological composition of claim 6 which induces a protective immune response and is thus a vaccine.

8. A method for inducing an immunological response in a host comprising administering a recombinant **TROVAC fowlpox** virus as claimed in any one of claims 1 to 5.

9. A method for inducing an immunological response in a host comprising administering an immunological composition as claimed in claims 6.

10. A method for inducing an immunological response in a host comprising administering an immunological composition as claimed in claims 7.

11. The method of claim 8 wherein the host is a chicken.

12. The method of claim 9 wherein the host is a chicken.

13. The method of claim 10 wherein the host is a chicken.

14. A method for expressing a gene product in vitro comprising contacting cells with a recombinant **TROVAC fowlpox** virus as claimed in any one of claims 1 to 5.

=> d

L4 ANSWER 1 OF 12 USPATFULL on STN
Full Text
AN 2005:292581 USPATFULL
TI Recombinant vaccine against West Nile Virus
IN Loosmore, Sheena May, Aurora, CANADA
Audonnet, Jean-Christophe Francis, Lyon, FRANCE
Minke, Jules Maarten, Corbas, FRANCE
PI US 2005255127 A1 20051117
AI US 2003-714781 A1 20031117 (10)
RLI Continuation-in-part of Ser. No. US 2003-679520, filed on 6 Oct 2003, PENDING Continuation-in-part of Ser. No. US 2003-374953, filed on 26 Feb 2003, PENDING Continuation-in-part of Ser. No. US 2002-116298, filed on 4 Apr 2002, ABANDONED Continuation-in-part of Ser. No. US 2003-676502, filed on 30 Sep 2003, PENDING Continuation of Ser. No. US 2003-374953, filed on 26 Feb 2003, PENDING Continuation-in-part of Ser. No. WO 2002-FR1200, filed on 5 Apr 2002, UNKNOWN
PRAI FR 2001-4737 20010406
US 2001-281923P 20010406 (60)
DT Utility
FS APPLICATION
LN.CNT 5985
INCL INCLM: 424/199.100
NCL NCLM: 424/199.100
IC [7]
ICM A61K039-12
IPCI A61K0039-12 [ICM,7]
IPCR A61K0039-12 [I,A]; A61K0039-12 [I,C]
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 15:39:03 ON 06 MAR 2006)

FILE 'USPATFULL' ENTERED AT 15:39:18 ON 06 MAR 2006
L1 116 S (FOWLPOX/CLM OR TROVAC/CLM)
L2 53 S L1 AND AY<2000
L3 6 S L2 AND (HIV/CLM OR GAG/CLM)

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=> s l1 and (cytokine/clm or interferon/clm)
          4834 CYTOKINE/CLM
          3944 INTERFERON/CLM
L5          15 L1 AND (CYTOKINE/CLM OR INTERFERON/CLM)

=> d l5,cbib,ab,clm,1-15

L5   ANSWER 1 OF 15  USPATFULL on STN
2005:261902 Combination therapy comprising a Cox-2 inhibitor and an
    antineoplastic agent.
    Masferrer, Jaime L., Ballwin, MO, UNITED STATES
    US 2005227929 A1 20051013
    APPLICATION: US 2004-989192  A1  20041115 (10)
    PRIORITY: US 2003-519701P  20031113 (60)
    DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     A method for treating or preventing neoplasia or a neoplasia-related
       disorder in a subject is provided, the method comprising administering
       to the subject an effective amount of a combination comprising a Cox-2
       inhibitor and an antineoplastic agent.
CLM    What is claimed is:
       1. A combination comprising a Cox-2 inhibitor and an antineoplastic
       agent in amounts effective when used in combination therapy for
       treatment or prevention of neoplasia or a neoplasia-related disorder;
       wherein the antineoplastic agent is selected from the group consisting
       of (1) polyglutamic acid-paclitaxel; (2) BMS-184476; (3) Paclimer
       microspheres with encapsulated paclitaxel; (4) taxane (IV) of Bayer;
       (5) BMS-188797; (6) epothilone B and analogs thereof including
       BMS-247550; (7) ILX-651; (8) N-[3-[(aminocarbonyl)amino]-4-
       methoxyphenyl]-2,3,4,5,6-pentafluorobenzenesulfonamide; (9) T-900607;
       (10) BAY 59-8862; (11) T-138067; (12) N,N-dimethyl-L-valyl-L-valyl-N-
       methyl-L-valyl-L-prolyl-N-(1,1-dimethylethyl)-L-prolinamide; (13)
       benzoylphenylurea; (14) trimetrexate glucuronate; (15)
       5-aza-2'-deoxycytidine; (16) tocladesine; (17) imatinib; (18)
       PTK-787; (19) BAY-439006; (20) N-[4-[(3-chloro-4-fluorophenyl)amino]-7-
       [3-(4-morpholinyl)propoxy]-6-quinazolinyl]-2-propenamide; (21)
       GW-572016; (22) EKB-569; (23) CP 609754; (24) CI-1033; (25) CCI-779;
       (26) BMS-214662; (27) (R)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-
       3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine-7-
       carbonitrile; (28) cilengitide; (29) bevacizumab; (30) PK-412; (31)
       IMC-1C11; (32) 1-(2-chloroethyl)-2-[(methylamino)]carbonyl}-2-
       (methylsulfonyl) hydrazide; (33) VNP-40101M; (34) camptothecin
       glycoconjugate; (35) liposome lurtotecan; (36) gallium maltolate;
       (37) N-[(3S,4E)-3-hydroxy-7-mercapto-1-oxo-4-heptenyl]-D-valyl-D-
       cysteinyl-(2Z)-2-amino-2-butenoyl-L-valine (4-1)-lactone cyclic (1-2)
       disulfide; (38) buthionine sulfoximine; (39) BMS-275291; (40)
       phenylacetate; (41) MS-275; (42) chloroquinoxaline sulfonamide; (43)
       INX-3280; (44) phosphorothioate antisense oligonucleotide; (45)
       GTI-2501; (46) GTI-2040; (47) K-ras protein vaccine; (48) K-ras
       antisense oligonucleotide; (49) MG-98; (50) liposome C-raf antisense
       oligonucleotide; (51) liposome raf-1 antisense oligonucleotide; (52)
       SPD-424; (53) Abarelix-depot; (54) ERA-923; (55) GTx-006; (56) ILX
       23-7553; (57) 2B1 bispecific MAb; (58) 3A1 MAb; (59) SS1(dsFv)-PE38;
       (60) chimeric TNT 1/B labeled with I-131; (61) MAb Hum291; (62)
       MEDI-507; (63) HumaRad-HN; (64) HumaRad-OV; (65) MAb humanized CD3;
       (66) Mylotarg; (67) MAb-CTLA-4; (68) cetuximab; (69) BEC2; (70)
       chimeric MAb 14.18; (71) anti-transferrin receptor MAb; (72)
       epratuzumab; (73) MGS rCEA; (74) INGN-241; (75) CV-787; (76)
       peripheral blood lymphocytes transduced with a gene encoding a chimeric
       T-cell receptor; (77) BCI Immune Activator; (78) Interferon-alpha
       gene therapy; (79) Xcellerate; (80) interleukin-2+staphylococcal
       enterotoxin B; (81) NBI-3001; (82) beta-alethine; (83) APC-8020;
       (84) interleukin-2/superantigen B gene combination; (85) Melacine
       vaccine; (86) SD/01; (87) ALVAC B7.1 vaccine; (88) APC-8024; (89)
       GnRH Pharmaccine vaccine; (90) rV-MUC-1; (91) HPV 16 E6 and E7 peptide
       vaccine; (92) allogeneic colon cancer vaccine; (93) allogeneic glioma
       vaccine; (94) autologous vaccine; (95) VHL peptide vaccine; (96)
       myeloma-derived idiotypic antigen vaccine; (97) CaPVax; (98) idiotype
       KLH lymphoma vaccine; (99) LHRH immunotherapeutic (synthetic peptide
       vaccine); (100) MAGE-12:170-178 peptide vaccine; (101) MART-1 melanoma
       vaccine; (102) MART-1 with gp100; (103) rF-tyrosine vaccine; (104)
       ESO-1:157-165 peptide vaccine; (105) fowlpox-CEA(6D) tricom and
       vaccinia-CEA(6D) tricom vaccine; (106) fowlpox gp100:ES 209-217 (2m)
       vaccine; (107) RAS 5-17 peptide vaccine; (108) proteinase-3 peptide
       vaccine; (109) canarypox CEA; (110) Helicobacter pylori vaccine;
       (111) P53 and RAS vaccine; (112) BAM-002; (113) MedPulser in
       combination with bleomycin; (114) lasofoxifene; (115) Filmix; (116)
       L-377202; (117) T4N5 Liposome Lotion; (118) Egr-1+TNF-alpha; (119)
       aprepitant; (120) skeletal targeted radiotherapy; (121)
       combretastatin; (122) CDC-501; (123) taurolidine; (124) Oramed;
       (125) nystatin; (126) Dynepo gene activated EPO; (127) NC-100150;
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(132) RK-0202; (133) SB-251353; (134) rasburicase; (135) AFP-scan; (136) Lymphoscan; (137) ADL 8-2698; (138) carboxypeptidase G2; (139) metoclopromide nasal; (140) dalteparin; (141) MK-869; (142) monomethyl arginine; (143) repifermin; (144) rH TPO; (145) SR-29142; (146) ancestin; (147) CP-461; (148) Bexxar; and combinations thereof.

2. The combination of claim 1 wherein the Cox-2 inhibitor is a Cox-2 selective inhibitor.

3. The combination of claim 2 wherein the Cox-2 selective inhibitor provides a Cox-1 $IC_{50/Cox-2}$ IC_{50} ratio of at least about 10.

4. The combination of claim 2 wherein the Cox-2 selective inhibitor provides a Cox-1 $IC_{50/Cox-2}$ IC_{50} ratio of at least about 100.

5. The combination of claim 2 wherein the Cox-2 selective inhibitor is a tricyclic compound, a substituted benzopyran derivative or a phenylacetic acid derivative.

6. The combination of claim 2 wherein the Cox-2 selective inhibitor is selected from the group consisting of celecoxib, valdecoxib, parecoxib, rofecoxib, etoricoxib, lumiracoxib and pharmaceutically acceptable salts thereof.

7. The combination of claim 2 wherein the Cox-2 selective inhibitor is parecoxib sodium.

8. A method of treating or preventing neoplasia or a neoplasia-related disorder in a subject, the method comprising administering in combination therapy to the subject a Cox-2 inhibitor and an antineoplastic agent in amounts effective when used in said combination therapy for treatment or prevention of neoplasia or a neoplasia-related disorder; wherein the antineoplastic agent is selected from the group consisting of (1) polyglutamic acid-paclitaxel; (2) BMS-184476; (3) Paclimer microspheres with encapsulated paclitaxel; (4) taxane (IV) of Bayer; (5) BMS-188797; (6) epothilone B and analogs thereof including BMS-247550; (7) ILX-651; (8) N-[3-[(aminocarbonyl)amino]-4-methoxyphenyl]-2,3,4,5,6-pentafluorobenzenesulfonamide; (9) T-900607; (10) BAY 59-8862; (11) T-138067; (12) N,N-dimethyl-L-valyl-L-valyl-N-methyl-L-valyl-L-prolyl-N-(1,1-dimethylethyl)-L-prolinamide; (13) benzoylphenylurea; (14) trimetrexate glucuronate; (15) 5-aza-2'-deoxycytidine; (16) tocladesine; (17) imatinib; (18) PTK-787; (19) BAY-439006; (20) N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]-6-quinazolinyl]-2-propenamide; (21) GW-572016; (22) EKB-569; (23) CP 609754; (24) CI-1033; (25) CCI-779; (26) BMS-214662; (27) (R)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine-7-carbonitrile; (28) cilengitide; (29) bevacizumab; (30) PK-412; (31) IMC-1C11; (32) 1-(2-chloroethyl)-2-[(methylamino)]carbonyl}-2-(methylsulfonyl) hydrazide; (33) VNP-40101M; (34) camptothecin glycoconjugate; (35) liposome lurtotecan; (36) gallium maltolate; (37) N-[(3S,4E)-3-hydroxy-7-mercapto-1-oxo-4-heptenyl]-D-valyl-D-cysteinyl-(2Z)-2-amino-2-butenoyl-L-valine (4-1)-lactone cyclic (1-2) disulfide; (38) buthionine sulfoximine; (39) BMS-275291; (40) phenylacetate; (41) MS-275; (42) chloroquinoxaline sulfonamide; (43) INX-3280; (44) phosphorothioate antisense oligonucleotide; (45) GTI-2501; (46) GTI-2040; (47) K-ras protein vaccine; (48) K-ras antisense oligonucleotide; (49) MG-98; (50) liposome C-raf antisense oligonucleotide; (51) liposome raf-1 antisense oligonucleotide; (52) SPD-424; (53) Abarelix-depot; (54) ERA-923; (55) GTx-006; (56) ILX 23-7553; (57) 2B1 bispecific MAb; (58) 3A1 MAb; (59) SS1(dsFv)-PE38; (60) chimeric TNT 1/B labeled with I-131; (61) MAb Hum291; (62) MEDI-507; (63) HumaRad-HN; (64) HumaRad-OV; (65) MAb humanized CD3; (66) Mylotarg; (67) MAb-CTLA-4; (68) cetuximab; (69) BEC2; (70) chimeric MAb 14.18; (71) anti-transferrin receptor MAb; (72) epratuzumab; (73) MGS rCEA; (74) INGN-241; (75) CV-787; (76) peripheral blood lymphocytes transduced with a gene encoding a chimeric T-cell receptor; (77) BCI Immune Activator; (78) **Interferon**-alpha gene therapy; (79) Xcellerate; (80) interleukin-2+staphylococcal enterotoxin B; (81) NBI-3001; (82) beta-alethine; (83) APC-8020; (84) interleukin-2/superantigen B gene combination; (85) Melacine vaccine; (86) SD/01; (87) ALVAC B7.1 vaccine; (88) APC-8024; (89) GnRH Pharmaccine vaccine; (90) rV-MUC-1; (91) HPV 16 E6 and E7 peptide vaccine; (92) allogeneic colon cancer vaccine; (93) allogeneic glioma vaccine; (94) autologous vaccine; (95) VHL peptide vaccine; (96) myeloma-derived idiotypic antigen vaccine; (97) CaPVax; (98) idiotype KLH lymphoma vaccine; (99) LHRH immunotherapeutic (synthetic peptide vaccine); (100) MAGE-12:170-178 peptide vaccine; (101) MART-1 melanoma vaccine; (102) MART-1 with gp100; (103) rF-tyrosine vaccine; (104) ESO-1:157-165 peptide vaccine; (105) **fowlpox**-CEA(6D) tricom and vaccinia-CEA(6D) tricom vaccine; (106) **fowlpox** gp100:ES 209-217 (2m) vaccine; (107) RAS 5-17 peptide vaccine; (108) proteinase-3 peptide

(111) P53 and RAS vaccine; (112) BAM-002; (113) MedPulser in combination with bleomycin; (114) lasofoxifene; (115) Filmix; (116) L-377202; (117) T4N5 Liposome Lotion; (118) Egr-1+TNF-alpha; (119) aprepitant; (120) skeletal targeted radiotherapy; (121) combretastatin; (122) CDC-501; (123) taurolidine; (124) Oramed; (125) nystatin; (126) Dynepo gene activated EPO; (127) NC-100150; (128) NC-100100; (129) CDC-801; (130) atrasentan; (131) Aranesp; (132) RK-0202; (133) SB-251353; (134) rasburicase; (135) AFP-scan; (136) Lymphoscan; (137) ADL 8-2698; (138) carboxypeptidase G2; (139) metoclopromide nasal; (140) dalteparin; (141) MK-869; (142) monomethyl arginine; (143) repifermin; (144) rH TPO; (145) SR-29142; (146) ancestin; (147) CP-461; (148) Bexxar; and combinations thereof.

9. The method of claim 8 wherein the Cox-2 inhibitor is a Cox-2 selective inhibitor.

10. The method of claim 9 wherein the Cox-2 selective inhibitor provides a Cox-1 $IC_{50/Cox-2}$ IC_{50} ratio of at least about 10.

11. The method of claim 9 wherein the Cox-2 selective inhibitor provides a Cox-1 $IC_{50/Cox-2}$ IC_{50} ratio of at least about 100.

12. The method of claim 9 wherein the Cox-2 selective inhibitor is a tricyclic compound, a substituted benzopyran derivative or a phenylacetic acid derivative.

13. The method of claim 9 wherein the Cox-2 selective inhibitor is selected from the group consisting of celecoxib, valdecoxib, parecoxib, rofecoxib, etoricoxib, lumiracoxib and pharmaceutically acceptable salts thereof.

14. The method of claim 9 wherein the Cox-2 selective inhibitor is parecoxib sodium.

15. The method of claim 8 wherein the Cox-2 inhibitor and the antineoplastic agent are administered sequentially.

16. The method of claim 8 wherein the Cox-2 inhibitor and the antineoplastic agent are administered substantially simultaneously.

17. The method of claim 8 wherein the neoplasia is selected from the group consisting of acral lentiginous melanoma, actinic keratosis, adenocarcinoma, adenoid cystic carcinoma, adenoma, adenosarcoma, adenosquamous carcinoma, adrenocortical carcinoma, AIDS-related lymphoma, anal cancer, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, bile duct cancer, bladder cancer, brain stem glioma, brain tumor, breast cancer, bronchial gland carcinoma, capillary carcinoma, carcinoids, carcinoma, carcinosarcoma, cavernous cell carcinoma, central nervous system lymphoma, cerebral astrocytoma, childhood cancers, cholangiocarcinoma, chondrosarcoma, chorioid plexus papilloma and carcinoma, clear cell carcinoma, colon cancer, colorectal cancer, cutaneous T-cell lymphoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal cancer, epithelioid carcinoma, esophageal cancer, Ewing's sarcoma, extragonadal germ cell tumor, fibrolamellar carcinoma, focal nodular hyperplasia, gallbladder cancer, gastrinoma, germ cell tumors, gestational trophoblastic tumor, glioblastoma, glioma, glucagonoma, hemangioblastoma, hemangioendothelioma, hemangioma, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, Hodgkin's lymphoma, hypopharyngeal cancer, hypothalamic and visual pathway glioma, insulinoma, interepithelial squamous cell neoplasia, intraepithelial neoplasia, intraocular melanoma, invasive squamous cell carcinoma, islet cell carcinoma, Kaposi's sarcoma, kidney cancer, large cell carcinoma, laryngeal cancer, leiomyosarcoma, lentigo maligna melanoma, leukemia-related disorders, lip and oral cavity cancer, liver cancer, lung cancer, lymphoma, malignant mesothelial tumors, malignant thymoma, medulloblastoma, medulloepithelioma, melanoma, meningeal carcinoma, merkel cell carcinoma, mesothelial carcinoma, metastatic carcinoma, mucoepidermoid carcinoma, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic syndrome, myeloproliferative disorders, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, neuroepithelial adenocarcinoma, nodular melanoma, non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial carcinoma, oral cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, ovarian germ cell tumor, pancreatic cancer, papillary serous adenocarcinoma, parathyroid cancer, penile cancer, pheochromocytoma, pineal and supratentorial primitive neuroectodermal tumors, pineal cell carcinoma, pituitary tumors, plasma cell neoplasm, plasmacytoma, pleuropulmonary blastoma, prostate cancer, pseudosarcoma, pulmonary blastoma, rectal cancer, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, small cell carcinoma, small intestine cancer, soft tissue carcinomas, somatostatin-secreting tumor, squamous cell carcinoma,

cancer, undifferentiated carcinoma, urethral cancer, uterine sarcoma, uveal melanoma, vaginal cancer, verrucous carcinoma, vipoma, vulvar cancer, Waldenstrom's macroglobulinemia, well differentiated carcinoma, and Wilm's tumor.

18. The method of claim 21, further comprising radiation therapy administered in combination with administration of the Cox-2 inhibitor and the antineoplastic agent.

19. A pharmaceutical composition comprising the combination of claim 1 and a pharmaceutically acceptable carrier.

20. A kit comprising a first dosage form that comprises an Cox-2 inhibitor in a first amount and a second dosage form that comprises an antineoplastic agent in a second amount; wherein said first and second amounts are effective when used in combination therapy for treating or preventing neoplasia or a neoplasia-related disorder; and wherein the antineoplastic agent is selected from the group consisting of (1) polyglutamic acid-paclitaxel; (2) BMS-184476; (3) Paclimer microspheres with encapsulated paclitaxel; (4) taxane (IV) of Bayer; (5) BMS-188797; (6) epothilone B and analogs thereof including BMS-247550; (7) ILX-651; (8) N-[3-[(aminocarbonyl)amino]-4-methoxyphenyl]-2,3,4,5,6-pentafluorobenzenesulfonamide; (9) T-900607; (10) BAY 59-8862; (11) T-138067; (12) N,N-dimethyl-L-valyl-L-valyl-N-methyl-L-valyl-L-prolyl-N-(1,1-dimethylethyl)-L-prolinamide; (13) benzoylphenylurea; (14) trimetrexate glucuronate; (15) 5-aza-2'-deoxycytidine; (16) tocladesine; (17) imatinib; (18) PTK-787; (19) BAY-439006; (20) N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]-6-quinazolinyl]-2-propenamide; (21) GW-572016; (22) EKB-569; (23) CP 609754; (24) CI-1033; (25) CCI-779; (26) BMS-214662; (27) (R)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine-7-carbonitrile; (28) cilengitide; (29) bevacizumab; (30) PK-412; (31) IMC-1C11; (32) 1-(2-chloroethyl)-2-[(methylamino)]carbonyl}-2-(methylsulfonyl) hydrazide; (33) VNP-40101M; (34) camptothecin glycoconjugate; (35) liposome lurtotecan; (36) gallium maltolate; (37) N-[(3S,4E)-3-hydroxy-7-mercapto-1-oxo-4-heptenyl]-D-valyl-D-cysteinyl-(2Z)-2-amino-2-butenoyl-L-valine (4-1)-lactone cyclic (1-2) disulfide; (38) buthionine sulfoximine; (39) BMS-275291; (40) phenylacetate; (41) MS-275; (42) chloroquinoxaline sulfonamide; (43) INX-3280; (44) phosphorothioate antisense oligonucleotide; (45) GTI-2501; (46) GTI-2040; (47) K-ras protein vaccine; (48) K-ras antisense oligonucleotide; (49) MG-98; (50) liposome C-raf antisense oligonucleotide; (51) liposome raf-1 antisense oligonucleotide; (52) SPD-424; (53) Abarelix-depot; (54) ERA-923; (55) GTx-006; (56) ILX 23-7553; (57) 2B1 bispecific MAb; (58) 3A1 MAb; (59) SS1(dsFv)-PE38; (60) chimeric TNT 1/B labeled with I-131; (61) MAb Hum291; (62) MEDI-507; (63) HumaRad-HN; (64) HumaRad-OV; (65) MAb humanized CD3; (66) Mylotarg; (67) MAb-CTLA-4; (68) cetuximab; (69) BEC2; (70) chimeric MAb 14.18; (71) anti-transferrin receptor MAb; (72) epratuzumab; (73) MGS rCEA; (74) INGN-241; (75) CV-787; (76) peripheral blood lymphocytes transduced with a gene encoding a chimeric T-cell receptor; (77) BCI Immune Activator; (78) **Interferon**-alpha gene therapy; (79) Xcellerate; (80) interleukin-2+staphylococcal enterotoxin B; (81) NBI-3001; (82) beta-alethine; (83) APC-8020; (84) interleukin-2/superantigen B gene combination; (85) Melacine vaccine; (86) SD/01; (87) ALVAC B7.1 vaccine; (88) APC-8024; (89) GnRH Pharmaccine vaccine; (90) rV-MUC-1; (91) HPV 16 E6 and E7 peptide vaccine; (92) allogeneic colon cancer vaccine; (93) allogeneic glioma vaccine; (94) autologous vaccine; (95) VHL peptide vaccine; (96) myeloma-derived idiotypic antigen vaccine; (97) CaPVax; (98) idiotype KLH lymphoma vaccine; (99) LHRH immunotherapeutic (synthetic peptide vaccine); (100) MAGE-12:170-178 peptide vaccine; (101) MART-1 melanoma vaccine; (102) MART-1 with gp100; (103) rF-tyrosine vaccine; (104) ESO-1:157-165 peptide vaccine; (105) **fowlpox**-CEA(6D) tricom and vaccinia-CEA(6D) tricom vaccine; (106) **fowlpox** gp100:ES 209-217 (2m) vaccine; (107) RAS 5-17 peptide vaccine; (108) proteinase-3 peptide vaccine; (109) canarypox CEA; (110) Helicobacter pylori vaccine; (111) P53 and RAS vaccine; (112) BAM-002; (113) MedPulser in combination with bleomycin; (114) lasofoxifene; (115) Filmix; (116) L-377202; (117) T4N5 Liposome Lotion; (118) Egr-1+TNF-alpha; (119) aprepitant; (120) skeletal targeted radiotherapy; (121) combretastatin; (122) CDC-501; (123) taurolidine; (124) Oramed; (125) nystatin; (126) Dynepo gene activated EPO; (127) NC-100150; (128) NC-100100; (129) CDC-801; (130) atrasentan; (131) Aranesp; (132) RK-0202; (133) SB-251353; (134) rasburicase; (135) AFP-scan; (136) Lymphoscan; (137) ADL 8-2698; (138) carboxypeptidase G2; (139) metoclopromide nasal; (140) dalteparin; (141) MK-869; (142) monomethyl arginine; (143) repifermin; (144) rH TPO; (145) SR-29142; (146) ancestin; (147) CP-461; (148) Bexxar; and combinations thereof.

2005:220914 Detection of mutations in a gene associated with resistance to viral infection, OAS1.
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Illumigen Biosciences, Inc., Seattle, WA, UNITED STATES (U.S. corporation)
US 2005191649 A1 20050901
APPLICATION: US 2004-972135 A1 20041022 (10)
PRIORITY: US 2003-513888P 20031023 (60)
US 2004-542373P 20040206 (60)
US 2004-554758P 20040319 (60)
US 2004-560524P 20040408 (60)
US 2004-578323P 20040609 (60)
US 2004-583503P 20040628 (60)
US 2004-605243P 20040826 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for detecting a mutation related to the gene encoding OAS1. This and other disclosed mutations correlate with resistance of humans to viral infection including hepatitis C. Also provided is a therapeutic agent consisting of a protein or polypeptide encoded by the mutated gene, or a polynucleotide encoding the protein or polypeptide. Inhibitors of human OAS1, including antisense oligonucleotides, methods, and compositions specific for human OAS1, are also provided.

CLM What is claimed is:

1. A human genetic screening method for identifying an oligoadenylate synthetase gene (OAS1) mutation comprising detecting in a nucleic acid sample the presence of an OAS1 point mutation selected from the group consisting of: substitution of a non-reference nucleotide for a reference nucleotide at nucleotide position 2135728, 2135749, 2135978, 2144072, 2144088, 2144116, 2144321, 2131025, 2133961, 2139587, 2144294, 2144985, 2156523, and 2156638 of reference sequence SEQ ED NO:19; and deletion of the reference nucleotide at position 2156595 of reference sequence SEQ ID NO:19; thereby identifying said mutation.

2. An isolated polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:20-30, SEQ ID NO:32-35, and SEQ ID NO:46-52.

3. An isolated polypeptide consisting of at least one amino acid sequence selected from the group consisting of SEQ ID NO:75-84 and having at least 80% sequence similarity to a polypeptide selected from the group consisting of SEQ ID NO:20-30, SEQ ID NO:32-35, and SEQ ID NO:46-52.

4. An isolated polypeptide consisting of at least one amino acid sequence selected from the group consisting of SEQ ID NO:75-84 and having at least 80% sequence similarity to a polypeptide selected from the group consisting of: (a) amino acids 219 through 238 of any one of SEQ ID NO:22 and SEQ ID NO:25; (b) amino acids 231 through 250 of SEQ ID NO:23; (c) amino acids 347 through 366 of any one of SEQ ID NO: 26-29, SEQ ID NO:33-34, and SEQ D NO:50; (d) amino acids 295 through 314 of SEQ ID NO:32; (e) amino acids 189 through 208 of SEQ ID NO:46; (f) amino acids 61 through 80 of SEQ ID NO:47.

5. The polypeptide of any one of claims 2-4 covalently attached to a polypeptide comprising a protein transduction domain.

6. The polypeptide of claim 5 wherein the protein transduction domain is comprised of a polypeptide selected from the group consisting of SEQ ID NO:85-94.

7. The polypeptide of claim 5 wherein the protein transduction domain is comprised of a polypeptide having at least 80% sequence similarity to a polypeptide selected from the group consisting of SEQ ID NO:85-94.

8. The polypeptide of claim 5 wherein the protein transduction domain differs from a polypeptide selected from the group consisting of SEQ ID NO:85-94 by the addition or substitution of an arginine, lysine, or histidine.

9. The polypeptide of any one of claims 2-8 covalently attached to polyethylene glycol.

10. The polypeptide of any one of claims 2-8 encapsulated in a liposome.

11. The polypeptide of any one of claims 2-8 covalently attached to an endosome disrupting agent.

12. The polypeptide of any one of claims 2-8 noncovalently attached to an endosome disrupting agent.

13. The polypeptide of claim 11 or 12 wherein the endosome disrupting agent is pH sensitive.

14. The polypeptide of any one of claims 2-13 covalently conjugated to a sugar moiety.

15. The polypeptide of claim 14 wherein the sugar moiety is comprised of galactose or mannose.

16. An isolated polypeptide produced by the method comprising: (a) expressing the polypeptide of any one of claims 2-8 by a cell; and (b) recovering said polypeptide.

17. The polypeptide of any one of claims 2-8 which is produced by a recombinant host cell.

18. The polypeptide of any one of claims 2-8 comprising a heterologous polypeptide sequence.

19. A composition comprising the polypeptide of any one of claims 2-18 and a pharmaceutically-acceptable carrier.

20. An isolated polynucleotide comprising a nucleotide sequence that encodes the polypeptide sequence of any one of claims 2-8.

21. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:31, SEQ ID NO:36-45 and SEQ ID NO:55-56.

22. A recombinant vector comprising the isolated polynucleotide of any one of claims 20 and 21.

23. An expression vector comprising the isolated polynucleotide of any one of claims 20 and 21, operably linked to an expression control sequence.

24. A host cell transformed or transfected with an expression vector according to claim 23.

25. An expression vector according to claim 23, wherein the vector is a viral vector.

26. An expression vector according to claim 23, wherein the vector is a viral vector selected from the group consisting of an adenovirus vector, adeno-associated virus vector, baculovirus, semliki forest virus vector, sindbis virus vector, pox virus vector, vaccinia virus vector, avian poxvirus vector, avipox virus vector, **fowlpox** virus vector, canarypox virus vector, alphavirus vector, **fowlpox** virus vector or lentivirus vector.

27. A composition comprising a first component selected from the group consisting of a pharmaceutically acceptable carrier, and a second component selected from the group consisting of an expression vector according to any one of claims 23, 25 and 26.

28. A method of treating viral infection in a mammal comprising administering to a mammal in need of such treatment a composition comprising oligoadenylate synthetase 1.

29. The method of claim 28 wherein said oligoadenylate synthetase 1 is the polypeptide of any one of claims 2-8.

30. The method of claim 28 wherein said oligoadenylate synthetase 1 is expressed by the polynucleotide of any one of claims 20 and 21.

31. The method of claim 28 comprising administering a composition according to any one of claims 19 and 27.

32. The method of claim 28 wherein said viral infection is an infection with a double-stranded RNA virus.

33. The method of claim 28 wherein said viral infection is an infection with a flavivirus.

34. The method of claim 33 wherein said flavivirus is the hepatitis C virus.

35. The method of claim 28 wherein said viral infection is an infection with a paramyxovirus.

36. The method of claim 28 wherein said viral infection is an infection with a virus selected from the group consisting of HIV, respiratory

measles, mumps, West Nile, dengue, yellow fever, polio, herpes, and human papilloma virus.

37. The method of claim 28 where said viral infection is severe acute respiratory syndrome.

38. The method of claim 28 wherein said mammal does not naturally produce said oligoadenylate synthetase 1.

39. A method of treating cancer in a mammal comprising administering to a mammal in need of such treatment a composition comprising oligoadenylate synthetase 1.

40. The method of claim 39 wherein said oligoadenylate synthetase 1 is the polypeptide of any one of claims 2-8.

41. The method of claim 39 wherein said oligoadenylate synthetase 1 is expressed by one of the polynucleotides of claims 20 and 21.

42. The method of claim 39 comprising administering a composition from any one of claims 19 and 27.

43. The method of claim 39 wherein said cancer is prostate cancer.

44. A monoclonal antibody directed against an epitope on a polypeptide of any one of claims 2-8.

45. The antibody of claim 44, wherein the antibody is not cross-reactive with another distinct polypeptide of any one of claims 2-8.

46. A composition comprising a pharmaceutically acceptable carrier and the antibody selected from any one of claims 44 and 45.

47. An isolated interfering polynucleotide that specifically binds with a target comprising the polynucleotide of any one of claims 20 and 21.

48. The interfering polynucleotide of claim 47 wherein the target binding site is at least 25 consecutive nucleotides.

49. A composition comprising the interfering polynucleotide of claim 47 and a pharmaceutical carrier.

50. An isolated antisense polynucleotide that specifically binds with SEQ ID NO:19.

51. A composition comprising the antisense polynucleotide of claim 50 and a pharmaceutical carrier.

52. An isolated ribozyme directed at a target comprising the polynucleotide of any one of claims 20 and 21.

53. A composition comprising the ribozyme of claim 52 and a pharmaceutical carrier.

54. A method of treating viral infection in a mammal comprising the step of inhibiting oligoadenylate synthetase 1 in a mammal in need of said treatment.

55. The method of claim 54 wherein said inhibiting oligoadenylate synthetase 1 comprises administering the composition of any of one of claims 46, 49, 51, 53, and 80.

56. The method of claim 54 wherein said oligoadenylate synthetase 1 is the polypeptide of any one of claims 2-8.

57. The method of claim 54 wherein said oligoadenylate synthetase 1 is expressed by the polynucleotide of any one of claims 20 and 21.

58. The method of claim 54 wherein said viral infection is infection with a virus selected from the group consisting of flavivirus, HIV, respiratory syncytial virus, influenza, coronavirus, parainfluenza, hepatitis A, measles, mumps, West Nile, dengue, yellow fever, polio, herpes, and human papilloma virus.

59. The method of claim 54 wherein said viral infection is severe acute respiratory syndrome.

60. A method of treating insulin dependent diabetes mellitus in a mammal comprising the step of inhibiting oligoadenylate synthetase 1 in a mammal in need of said treatment.

61. The method of claim 60 wherein said oligoadenylate synthetase 1 is

62. The method of claim 60 wherein said oligoadenylate synthetase 1 is expressed by the polynucleotide of any one of claims 20 and 21.

63. The method of claim 60 wherein said inhibiting oligoadenylate synthetase 1 comprises administering a composition from any one of claims 46, 49, 51, 53 and 80.

64. The method of claim 1, wherein the screening method identifies susceptibility to viral infection in said human.

65. The method of claim 1 wherein the screening method identifies predisposition to diabetes mellitus in said human.

66. The method of claim 1, wherein the screening method identifies predisposition to schizophrenia in said human.

67. The method of claim 1, wherein the screening method identifies susceptibility to cancer in said human.

68. The method of claim 67, wherein the cancer is prostate cancer.

69. The method of claim 1, wherein the screening method identifies patient responsiveness to therapeutic treatments for viral infection.

70. The method of claim 69 wherein the therapeutic treatment is **interferon**-based.

71. The method of claim 69 wherein patient response is measured by sustained viral clearance.

72. A method for treating schizophrenia in a human comprising the step of inhibiting oligoadenylate synthetases 1 in a human in need of said treatment.

73. The method of claim 72 wherein said oligoadenylate synthetase 1 is the polypeptide of any one of claims 2-8.

74. The method of claim 72 wherein said oligoadenylate synthetase 1 is expressed by the polynucleotide of any one of claims 20 and 21.

75. The method of claim 72 wherein said inhibiting oligoadenylate synthetase 1 comprises administering a composition from any one of claims 46, 49, 51, 53 and 80.

76. The method of claim 72 wherein said inhibitor comprises a small molecule drug.

77. The method of claim 54 wherein said inhibitor comprises a small molecule drug.

78. The method of claim 60 wherein said inhibitor comprises a small molecule drug.

79. An antibody fragment developed from a monoclonal antibody directed against an epitope on a polypeptide of any one of claims 2-8.

80. A composition comprising a pharmaceutically acceptable carrier and the antibody fragment of claim 79.

81. The method of claim 1, wherein the screening method identifies susceptibility to hepatitis C infection in said human.

L5 ANSWER 3 OF 15 USPATFULL on STN
2005:158194 Novel mhc class II restricted t cell epitopes from the cancer antigen, ny eso-1.
Wang, Rong-Fu, Houston, TX, UNITED STATES
Rosenberg, Steven A., Potomac, MD, UNITED STATES
Zeng, Gang, Germantown, MD, UNITED STATES
US 2005136402 A1 20050623
APPLICATION: US 2002-182506 A1 20010126 (10)
WO 2001-US2765 20010126
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses the identification and isolation of novel MHC class II epitopes derived from the cancer antigen, NY ESO-1. The novel MHC class II epitopes from NY-EsO-1 are recognized by CD4+ T lymphocytes in an HLA class II restricted manner, in particular HLA-DR or HLA-DP restricted. The products of the gene are promising candidates for immunotherapeutic strategies for the prevention, treatment and diagnosis of patients with cancer.

1. An NY-ESO-1 cancer peptide or MHC class II restricted T cell epitope, functional portion, variants or derivatives thereof encoded within a nucleic acid sequence consisting SEQ. ID NO: 1 and variants thereof.

2. An MHC class II restricted T cell epitope of NY-ESO-1, function portion or derivative according to claim 1 wherein the epitope is encoded by a sequence consisting of SEQ. ID NO: 2, homologs or functional portion thereof.

3. An MHC class II restricted T cell epitope of NY-ESO-1, fuctional portion or derivative according to claim 1 wherein the peptide is encoded by a sequence consisting of SEQ. ID NO: 27 or portion thereof.

4. An MHC class II restricted T cell epitope of NY-ESO-1 comprising at least one of SEQ. ID NO: 4-21, 29-34, functional portion, derivative or combination thereof.

5. An MHC class II restricted T cell epitope of NY-ESO-1 according to claim 4 wherein the epitope is selected from the group consisting of SEQ ID NO: 5 through SEQ ID NO: 18, functional portion, derivative or combination thereof.

6. An MHC class II restricted T cell epitope of NY-ESO-1 according to claim 4 wherein the epitope comprises VLLKEFTVSG (SEQ ID NO: 19), variant or derivative thereof.

7. An MHC class II restricted T cell epitope of NY-ESO-1 according to claim 1-5 or 6 wherein the epitope is immunologically recognized by HLA-DR restricted T lymphocytes.

8. An MHC class II restricted T cell epitope of NY-ESO-1 according to claim 1-5 or 6 wherein the T lymphocytes are CD4+.

9. An MHC class II restricted T cell epitope of NY-ESO-1 according to claim 4 wherein the cancer peptide is derived from a cancer selected from the group consisting of: a non-Hodgkins lymphoma, leukemia, Hodgkins lymphoma, lung cancer, liver cancer, metastases, melanoma, head cancer, neck cancer, neuroblastoma, adenocarcinoma, thymoma, colon cancer, uterine cancer, breast cancer, prostate cancer, ovarian cancer, cervical cancer, bladder cancer, kidney cancer, pancreatic cancer and sarcoma.

10. A MHC class II restricted T cell epitope of NY-ESO-1 according to claim 4 wherein the epitope is encoded by a nucleic acid sequence comprising AAG GAG UTC ACT GTG TCC (SEQ. ID NO: 28).

11. A pharmaceutical composition comprising at least one MHC class II restricted T cell epitope of NY-ESO-1 according to claims 1-9 or 10 and a pharmaceutically acceptable carrier.

12. A pharmaceutical compositon according to claim 11 wherein the composition further comprises an immunostimulatory molecule.

13. The pharmaceutical compostion according to claim 12 wherein the immunostimulatory molecule is on HLA-class II molecule or cell expressing an HLA class II molecule.

14. A pharmaceutical composition according to claim 11, wherein the composition further comprises B7.1, B7.2, ICAM-1, ICAM-2, LFA-1, LFA-3, **cytokine** or combinations thereof.

15. A pharmaceutical composition according to claim 11, wherein the composition further comprises at least one MHC class I restricted T cell epitope of NY-ESO-1.

16. The pharmaceutical composition according to claim 15 wherein the MHC class I restricted T cell epitope comprises SEQ ID NO: 22 or SEQ ID NO: 23.

17. A immunogen comprising at least one MHC class II restricted T cell epitope of NY-ESO-1 according to claims 1-9 or 10 alone or in combination, and optionally at least one immunostimulatory molecule.

18. A immunogen according to claim 17 wherein the immunostimulatory molecule is an HLA class II molecule.

19. A immunogen according to claim 17, further comprising an MHC class I restricted T cell epitope of NY-ESO-1.

20. A immunogen according to claim 19 wherein the MHC class II restricted T cell epitope and the MHC class I restricted T cell epitope are linked together via a peptide bond.

21. An isolated nucleic acid sequence comprising SEQ ID NO: 27, functional portion or homolog thereof said sequence encoding at least one MHC class II restricted T cell epitope.

22. An isolated nucleic acid sequence according to claim 21 wherein the nucleic acid sequence is selected from the group consisting of SEQ ID NO.: 24, 25, 26 or portion or variant thereof.

23. An isolated nucleic acid sequence which encodes at least one MHC class II restricted T cell epitope of NY-ESO-1 comprising an amino acid sequence of any one of SEQ ID NO: 4-21, 29-34, combinations, functional portion or derivative thereof.

24. An isolated nucleic acid sequence of claim 23 further comprising a nucleic acid sequence which encodes at least one MHC class I restricted T cell epitope of NY-ESO-1.

25. A recombinant expression vector comprising the nucleic acid sequence according to claims 21, 22, 23 or 24.

26. A host organism transformed or transfected with a recombinant expression vector according to claim 25.

27. A host organism according to claim 26 wherein the host organism is an antigen presenting cell.

28. An oligonucleotide consisting of a nucleic acid sequence complementary to the nucleic acid sequence according to claims 21, 22 or 23.

29. A recombinant virus comprising the nucleic acid sequence according to claims 21, 22, 23 or 24.

30. The recombinant virus according to claim 29 wherein the virus is selected from the group consisting of retrovirus, baculovirus, Ankara virus, **fowlpox**, adenovirus, vaccinia virus, lentivirus, and replicase-based alphavirus.

31. A recombinant virus according to claim 29 further comprising at least one gene encoding an immunostimulatory molecule.

32. A recombinant virus according to claim 31 wherein the immunostimulatory molecule is a HLA class II molecule.

33. A host organism transformed or transfected with the recombinant virus according to claim 29-31 or 32.

34. An isolated antibody or antigen binding portion thereof that binds the MHC class II restricted T cell epitope of NY-ESO-1 according to claims 1-5 or 6.

35. A method of producing a recombinant MHC class II restricted T cell epitope of NY-ESO-1 thereof comprising: a. inserting a nucleotide sequence according to claims 21, 22 or 23, functional portion or variant thereof, into an expression vector; b. transferring the expression vector into a host cell; c. culturing the host cell under conditions appropriate for expression of the epitope or functional portion thereof; and d. harvesting the recombinant epitope, or functional portion thereof.

36. A method according to claim 35 further comprising in step (a) inserting a nucleotide sequence encoding an HLA class II molecule, or portion thereof into the expression vector.

37. A method of detecting the presence of cancer or precancer in a mammal comprising: a. contacting a nucleic acid sequence according to claims 21, 22 or 23, functional portion or variant thereof with a test biological sample of mRNA taken from the mammal under conditions allowing for a complex to form between the sequence and the mRNA; b. detecting the complex; c. comparing the amount of mRNA in the test sample with an amount of mRNA from a known normal biological sample, wherein an increased amount of mRNA from the test sample is indicative of cancer or precancer.

38. A method according to claim 37 wherein the cancer or precancer is melanoma.

39. A method of detecting an MHC class II restricted T cell epitope of NY-ESO-1 or portion thereof in a biological sample comprising: a. contacting the sample with antibody or antigen binding portion thereof specific for said epitope according to claim 34 under conditions to form an immune complex between said antibody and epitope, and b. detecting

epitope in the biological sample.

40. A method of preventing or inhibiting cancer in a mammal comprising: administering to the mammal an effective amount of at least one MHC class II restricted T cell epitope of NY-ESO-1, or functional portion thereof according to claims 1-5 or 6, alone or in combination with an HLA class I molecule, said amount is effective in preventing or inhibiting the cancer in the mammal.

41. The method according to claim 40, further comprising administration of at least one MHC class I restricted T cell epitope of NY-ESO-1.

42. A method of inhibiting melanoma in a mammal comprising: a. exposing T lymphocytes in vitro to at least one MHC class II restricted T cell epitope of NY-ESO-1, or functional portion thereof according to claims 1-5 or 6, alone or in combination with an MHC class II molecule for a time sufficient to elicit SMC class II restricted T lymphocytes; b. administering the MHC class II restricted T lymphocytes to the mammal alone or in combination with at least one MHC class II restricted T cell epitope of NY-ESO-1, functional portion thereof or a native NY-ESO-1 protein in an amount sufficient to inhibit the melanoma.

43. A method of preventing or inhibiting cancer in a mammal comprising administering to the mammal an effective amount of a recombinant virus according to claim 29 alone or in combination with an exogenous immunostimulatory molecule said amount is effective in preventing or inhibiting the cancer.

44. A method according to claim 43 wherein the mammal expresses an HLA Class II DR molecule.

45. The method according to claim 43 further comprising the administration of a recombinant virus encoding au MHC class I restricted T cell epitope of NY-ESO-1.

46. A pharmaceutical composition comprising the recombinant virus according to claim 29 alone or in combination with an exogenous immunostimulatory molecule, chemotherapy drug, antibiotic, antifungal drug, antiviral drug or combination thereof and a pharmaceutically acceptable carrier.

47. A transgenic animal carrying and expressing a gene encoding at least one MHC class II restricted T cell epitope of NY-ESO-1 comprising at least a fragment of SEQ ID NO: 27, or functional portion or variant thereof.

48. A cancer antigen specific human CD4+ T lymphocyte elicited by the MHC class II restricted T cell epitope of NY-ESO-1 according to claim 1-5 or 6.

49. The cancer antigen specific human CD4+ T lymphocyte according to claim 48, wherein the lymphocyte recognizes an HLA-class II molecule.

50. The cancer antigen specific human CD4+ T lymphocyte according to claim 48, wherein the lymphocyte recognizes an HLA-DR molecule.

51. A cancer peptide according to claim 1, wherein the peptide comprising the amino acid motif: Xaa_{1I} TQ Xaa_2 FXaa_{3P} Xaa_4 (SEQ ID NO: 51) and homologs thereof, wherein Xaa_1, Xaa_2, Xaa_3, and Xaa_4 are each at least one amino acid, said peptide is immunologically recognized by HLA-DP restricted CD4+ T lymphocytes.

52. The cancer peptide according to claim 51, wherein Xaa_1 is selected from the group consisting of Tip, Phe, Tyr, Met, Ile, Val, Ala; and combinations thereof.

53. The cancer peptide according to claim 51, wherein Xaa_2 is selected from the group consisting of Cys, Ser, Val, Ala, Thr; and combinations thereof.

54. The cancer peptide according to claim 51, wherein Xaa_3 is selected from the group consisting of Leu, Phe, Tyr, Met, Ile, Val, Ala; and combinations thereof.

55. The cancer peptide according to claim 51, wherein Xaa_4 is selected from the group consisting of Val, Tyr, Ile, Ala, Leu, Pro and combinations thereof.

56. The cancer peptide according to claim 51, wherein the peptide comprises about 9 to about 30 amino acids.

comprises about 10 to about 20 amino acids.

58. The cancer peptide according to claim 51, wherein the peptide comprises about 10 to about 15 amino acids.

59. The cancer peptide according to claim 51, wherein the homolog is derived from a LAGE gene.

60. A cancer peptide according to claim 51, wherein the peptide comprises the amino acid sequence: Xaa_1 WITQCFLPVF-Xaa_2 (SEQ ID NO: 52); and variants thereof wherein Xaa_1 and Xaa_2 are each no amino acid or one or more naturally occurring amino acids.

61. The cancer peptide according to claim 60, wherein the peptide comprises about 10 to about 30 amino acids.

62. The cancer peptide according to claim 60, wherein the peptide comprises about 10 to about 20 amino acids.

63. The cancer peptide according to claim 60, wherein the peptide comprises about 10 to about 15 amino acids.

64. A cancer peptide according to claim 60, wherein said peptide consists of W I T Q C F L P V F (SEQ ID NO: 80).

65. The cancer peptide of claim 1, wherein said peptide comprises L L M W I T Q C F L P V F L (SEQ ID NO: 55), L M W I T Q C F L P V F L A (SEQ ID NO: 56), M W I T Q C F L P V F L A Q (SEQ ID NO: 57) and W I T Q C F L P V F L A Q P (SEQ IDNO 58).

66. The peptide of claim 51, wherein the peptide is immunologically recognized by HLA-DPB1*0401-0402 restricted CD4+ T-lymphocytes.

67. The peptide of claim 51, wherein the peptide is linked to a carrier protein.

68. The peptide of claim 67, wherein the carrier protein is selected from the group consisting of KLH, tetanus toxoid and albumin.

69. An isolated nucleic acid sequence encoding the peptide of claims 51, 60, 64 or 65.

70. An isolated nucleic acid sequence encoding at least one MHC class II restricted T cell epitope peptide comprising any one of SEQ ID NOS: 53, 55 through 64, or combinations thereof.

71. An isolated polynucleotide comprising a nucleic acid sequence which hybridizes under stringent conditions with the nucleic acid sequence according to claims 69 or 70.

72. A cancer peptide having an amino acid motif S L L M W I T Q C F L P V F (SEQ ID NO: 54), or variant thereof, said peptide is immunologically recognized by both HLA-DP restricted CD4+ T lymphocytes and MHC class I restricted CD8+ T-lymphocytes.

73. The cancer peptide according to claim 72, wherein the variant has an addition of an arginine residue at the amino terminus.

74. The cancer peptide according to claim 72, wherein the variant has an argirine substituted in place of phenylalanine at the carboxyl terminus.

75. The peptide according to claim 72, wherein the peptide is immunologically recognized by HLA-DPB 1*0401-0402 restricted T-lymphocytes and HLA-A2 restricted T-lymphocytes.

76. An isolated nucleic acid sequence encoding the peptide of claim 72.

77. An isolated nucleic acid sequence encoding the peptide of SEQ ID NO: 54.

78. An isolated polynucleotide comprising a nucleic acid sequence which hybridizes under stringent conditions with the nucleic acid sequence according to claims 76 or 77.

79. A recombinant expression vector comprising the nucleic acid sequence according to claim 69.

80. A recombinant expression vector comprising the nucleic acid sequence according to claim 70.

81. A recombinant expression vector comprising the nucleic acid sequence according to claim 76.

82. A recombinant expression vector comprising the nucleic acid sequence according to claim 77.

83. The recombinant expression vector according to any one of claims 79-82, further comprising a nucleic acid sequence encoding at least one NY-ESO-1 HLA-DR restricted T cell cancer peptide.

84. The recombinant expression vector according to claim 83, wherein the NY-ESO-1 HLA DR restricted T cell cancer peptide comprises an amino acid sequence selected from the group consisting of:

LPVPGVLLKEFTVSG; (SEQ ID NO: 10)

VLLKEFTVSGNILTIRLT; (SEQ ID NO: 65)

AADHRQLQLSISSCLQQL; (SEQ ID NO: 66)

and combinations thereof.

85. The recombinant expression vector according to claim 83, further comprising a nucleic acid sequence encoding at least one isolated NY-ESO-1 HLAlass I restricted T cell cancer peptide.

86. The recombinant expression vector according to claim 85, wherein the NY-ESO-1 HLA-class I restricted T cell cancer peptide comprises: Xaa_1 Xaa_2 Xaa_3 GPGGGAP Xaa_4 (SEQ ID NO: 22); wherein Xaa_1 is no amino acid or one to about 20 naturally occurring amino acids: Xaa_2 is Ale, Thr, Val, Leu or Arg; Xaa_3 is Ser or a conservative substitution; Xaa_4 is Arg or Lys; and derivatives thereof.

87. The recombinant expression vector according to claim 86, wherein the nucleic acid sequence encodes ASGPGGGAPR (SEQ ID NO: 23).

88. A host cell or host organism transformed or transfected by the vector according to any one of claims 79-87.

89. A recombinant virus encoding at least one cancer peptide according to any one of claims 51, 60, 64, 65, or 72.

90. A host cell or host organism transformed by the recombinant virus according to claim 89.

91. A recombinant virus comprising an isolated nucleic acid sequence encoding at least one MHC class II restricted T cell epitope peptide comprising any one of SEQ ID NO: 51-64, 80 or combinations thereof.

92. The recombinant virus according to claim 91, wherein the recombinant virus is selected from die group consisting of vaccinia, **fowlpox**, adenovirus, retrovims, lentivirus, baculovirus, Ankaravirus, and replicase-based alphavirus.

93. The recombinant virus according to claim 91, further comprising a nucleic acid sequence encoding an HLA-DP molecule.

94. The recombinant virus according to claim 91, further comprising a nucleic acid sequence encoding at least one NY-ESO-1 HLA-DR restricted T cell cancer peptide.

95. The recombinant virus according to claim 94, wherein the NY-ESO-1 HLA DR restricted T cell cancer peptide comprises an amino acid sequence selected from the group consisting of:

LPVPGVLLKEFTVSG; (SEQ ID NO: 10)

VLLKEFTVSGNILTIRLT; (SEQ ID NO: 65)

AADHRQLQLSISSCLQQL; (SEQ ID NO: 66)

variants, and combinations thereof.

96. The recombinant virus according to claim 91, further comprising a nucleic acid sequence encoding at least one isolated NY-ESO-1 HLA-class I restricted T cell cancer peptide.

97. The recombinant virus according to claim 96, wherein the NY-ESO-1 HLA-class I restricted T cell cancer peptide comprises: Xaa_1 Xaa_2 Xaa_3 GPGGGAP Xaa_4 (SEQ ID NO. 22); wherein Xaa_1 is no amino acid or one to about 20 naturally occurring amino acids: Xaa_2 is Ale, Thr, Val, Leu or Arg; Xaa_3 is Ser or a conservative substitution; Xaa_4 is Arg or Lys; and derivatives

98. The recombinant expression vector according to claim 97, wherein the nucleic acid sequence encodes a peptide comprising the amin acid sequence ASGPGGGAPR (SEQ ID NO: 23).

99. A host cell or host organism transformed or transfected by the virus according to any one of claims 91-98.

100. A host cell or host organism according to claim 99, further comprising a nucleic acid sequence encoding an HLA-DP molecule.

101. A pharmaceutical composition comprising the peptide according to any one of claims 51, 60, 64 or 65 and a pharmaceutically acceptable carrier.

102. A pharmaceutical composition comprising the peptide according to claim 72 and a pharmaceutically acceptable carrier.

103. A pharmaceutical composition comprising the recombinant expression vector according to any one of claims 79-87 and a pharmaceutically acceptable carrier.

104. A pharmaceutical composition comprising the recombinant virus according to any one of claims 91-95 and a pharmaceutically acceptable carrier.

105. The pharmaceutical composition according to claim 101, wherein the composition further comprises an immunostimulatory molecule.

106. The pharmaceutical composition according to claim 105, wherein the immunostimulatory molecule is B7.1, B7.2, ICAM-1, ICAM-2, LFA-1, LFA-3, **cytokine** or combinations thereof.

107. The pharmaceutical composition according to claim 101, further comprising an HLA-class II molecule or cell expressing an HLA-class II molecule.

108. The pharmaceutical composition according to claim 107, wherein the HLA-class II molecule is HLA-DP.

109. The pharmaceutical composition according to claim 108, wherein the HLA-class II molecule is HLA-DPB1*0401-0402.

110. The pharmaceutical composition according to claim 101, further comprising at least one NY-ESO-1 HLA-DR restricted T cell cancer peptide.

111. The pharmaceutical composition according to claim 110, wherein the NY-ESO-1 HLA DR restricted T cell cancer peptide comprises an amino acid sequence selected from the group consisting of:

LPVPGVLLKEFTVSG; (SEQ ID NO: 10)

VLLKEFTVSGNILTIRLT; (SEQ ID NO: 65)

AADHRQLQLSISSCLQQL; (SEQ ID NO: 66)

and combinations thereof.

112. The pharmaceutical composition according to claim 101, further comprising at least one isolated NY-ESO-1 HLA class I restricted T cell cancer peptide.

113. The pharmaceutical composition according to claim 112, wherein the NY-ESO-1 HLA class I restricted T cell cancer peptide comprises: Xaa_1 Xaa_2 Xaa_3 GPGGGAPXaa_4 (SEQ ID NO: 22); wherein Xaa_1 is no amino acid or one to about 20 naturally occurring amino acids; Xaa_2 is Ala, Thr, Val, Leu or Arg; Xaa_3 is Ser or a conservative substitution; Xaa_4 is Arg or Lys; and derivatives thereof.

114. The pharmaceutical composition according to claim 113, wherein the NY-ESO-1 HLA class I restricted T cell cancer peptide comprises: ASGPGGGAPR (SEQ ID NO: 23).

115. A pharmaceutical composition comprising the nucleic acid sequence according to any one of claims 69, 70, 76 or 77 and a pharmaceutically acceptable carrier

116. An immunogen comprising the cancer peptide according to any one of claims 51, 60, 64, 65 or 72 which elicits NY-ESO-1 HLA-DP restricted CD4+ T lymphocytes.

117. The immunogen according to claim 116, which elicits an anti-NY-ESO-1 antibody.

118. The immunogen according to claim 116, further comprising an adjuvant.

119. The immunogen according to claim 116, wherein the peptide is linked to a carrier protein.

120. A cancer vaccine comprising the cancer peptide according to any one of claims 51, 60, 64, 65 or 72.

121. An isolated antibody or antigen binding portion thereof that binds the HLA-DP restricted T cell epitope of NY-ESO-1 according to any one of claims 51, 60, 64, 65 or 72.

122. An antibody according to claim 121, wherein said antibody is a polyclonal antibody.

123. An antibody according to claim 121, wherein said antibody is a monoclonal antibody.

124. An antibody according to claim 121, wherein said antibody is labeled with a detectable label.

125. An antibody according to claim 121, wherein said detectable label is a radioactive isotope.

126. An antibody according to claim 121, wherein the antibody is modified by addition of a cytotoxic or cytostatic drug.

127. A pharmaceutical composition comprising the antibody according to claim 121 and a pharmaceutically acceptable carrier.

128. A kit comprising the antibody according to claim 121.

129. The kit according to claim 128, further comprising immunoassay reagents.

130. The antibody or antigen binding portion thereof according to claim 121, wherein the antibody further binds to an HLA-DP molecule.

131. A method of producing a recombinant HLA-DP restricted CD4+ T cell epitope of NY-ESO-1 thereof comprising: a. inserting a nucleotide sequence encoding at least one of SEQ ID NOS. 51-64, 80 or portion or variant thereof, into an expression vector; b. transferring the expression vector into a host cell; c. culturing the host cell under conditions appropriate for expression of the epitope or portion thereof; and d. harvesting the recombinant epitope, or portion thereof.

132. A method according to claim 131, further comprising in step (a) inserting a nucleotide sequence encoding an HLA class II molecule, or portion thereof into the expression vector.

133. The method according to claim 132, wherein the HLA class II molecule is HLA-DP.

134. A method of making a vector which expresses a cancer peptide comprising the amino acid sequence of at least one of SEQ ID NOS: 51-64 or 80, said method comprises incorporating an isolated nucleic acid sequence encoding at least one of SEQ ID NOS: 51-64 or 80 operatively linked with a promoter.

135. A method of detecting the presence of cancer or precancer in a mammal comprising: a. contacting a nucleic acid sequence encoding at least one of SEQ ID NOS.: 51-64 or 80 or portion or variant thereof with a test biological sample of mRNA taken from the mammal under conditions allowing for a complex to form between the sequence and the mRNA; b. detecting the complex; c. comparing the amount of in RNA in the test sample with an amount of mRNA from a known normal biological sample, wherein an increased amount of mRNA from the test sample is indicative of cancer or precancer.

136. A method according to claim 135, wherein the cancer or precancer is melanoma.

137. A method of detecting the presence of cancer or precancer in a mammal comprising: a) contacting a cancer peptide according to claims 51, 60, 64, 65 or 72 with a test biological sample of lymphocytes obtained from said mammal; b) detecting CD4+ T lymphocytes immunoreactive with the cancer peptide, wherein an increased number of CD4+ T lymphocytes immunoreactive with the cancer peptide in comparison

138. A method of detecting the HLA-DP restricted CD4+ T cell epitope of NY-ESO-1 or portion thereof in a biological sample comprising: a. contacting the sample with antibody or antigen binding portion thereof specific for said epitope according to any one of claims 121-125 under conditions to form an immune complex between said antibody and epitope, and b. detecting the presence of the immune complex, said presence indicative of the epitope in the biological sample.

139. A method of preventing or inhibiting cancer in a mammal comprising: administering to the mammal an effective amount of the HLA-DP restricted T cell epitope of NY-ESO-1, or portion thereof according to claims 51, 60, 64, 69 or 72, alone or in combination with an HLA-DP molecule, said amount is effective in preventing or inhibiting the cancer in the mammal.

140. The method according to claim 139, wherein the HLA-DP molecule is HLA-DPB*0401-0402.

141. The method according to claim 139, further comprising administration of an HLA-DR restricted T cell epitope of NY-ESO-1, alone or in combination with an HLA-DR molecule.

142. The method according to claim 141, wherein the HLA-DR restricted T cell epitope of NY-ESO-1 comprises at least one of SEQ ID NOS: 10, 65 or 66.

143. The method according to claim 139, further comprising administration of an HLA class I restricted T cell epitope of NY-ESO-1.

144. The method according to claim 143, wherein the HLA class I restricted T cell epitope comprises SEQ ID NOS: 22 or 23.

145. A method of inhibiting growth of a tumor expressing NY-ESO-1 comprising administration of an amount of the cancer peptide according to any one of claims 51, 60, 64, 65 or 72, said amount is effective in inhibiting the growth of the tumor expressing NY-ESO-1.

146. A method of inhibiting melanoma in a mammal comprising: a. exposing T lymphocytes in vitro to an HLA-DP restricted T cell cancer peptide of NY-ESO-1, or portion thereof according to any one of claims 51, 60, 64, 65 or 72, alone or in combination with an HLA-DP molecule for a time sufficient to elicit NY-ESO-1 HLA-DP restricted T lymphocytes; b. administering the T lymphocytes to the mammal in an amount sufficient to inhibit the melanoma.

147. The method according to claim 146, filer comprising administering the cancer peptide or native NY-ESO-1 protein to the mammal.

148. A method of preventing or inhibiting cancer in a mammal comprising administering to the mammal an effective amount of a recombinant virus according to claim 91 alone or in combination with an exogenous immunostimulatory molecule said amount is effective in preventing or inhibiting the cancer.

149. A method according to claim 148, wherein the mammal expresses an HLA-DP molecule.

150. The method according to claim 148, further comprising the administration of a recombinant virus encoding an MHC class I restricted T cell epitope of NY-ESO-1.

151. A method of inhibiting tumor growth of a tumor expressing NY-ESO-1 comprising administration of an amount of the nucleic acid according to any one of claims 69, 70, 76 or 77, said amount is effective in or inhibiting the growth of the tumor.

152. A pharmaceutical composition comprising the recombinant virus according to claim 91 alone or in combination with an exogenous immunostimulatory molecule, chemotherapy drug, antibiotic, antifungal drug, antiviral drug or combination thereof and a pharmaceutically acceptable carrier.

153. A transgenic animal carrying and expressing a gene encoding an HLA-DP restricted CD4+ T cell epitope of NY-ESO-1 comprising at least one of SEQ ID NOS: 51-64, 80, or functional portion thereof.

154. A cancer antigen specific human CD4+ T lymphocyte immunoreactive with an HLA-DP restricted T cell epitope of NY-ESO-1 according to claims 51, 60, 64, 65 or 72.

155. The cancer antigen specific human CD4+ T lymphocyte according

molecule.

156. A target antigen-cancer peptide carrier conjugate comprising a target antigen or target epitope thereof linked to cancer peptide carrier comprising at least one of SEQ ID NO: 51-64 or 80.

157. The target antigen-cancer peptide carrier conjugate according to claim 156 wherein the target antigen is selected from the group consisting of TRP2, GP-100, TRP1, HIV antigens, gp120, malaria antigens and epitopes thereof.

158. A nucleic acid vaccine construct comprising a nucleic acid sequence encoding a cancer peptide carrier comprising at least one of SEQ ID NO: 51-64 or 80 and at least one nucleic acid sequence encoding a target antigen or target epitope thereof.

159. The nucleic acid vaccine construct according to claim 158 wherein the target antigen or target epitope thereof is selected from the group consisting of TRP2, GP-100, TP, HIV antigens, gp120, malaria antigens and epitopes thereof.

160. A method of inhibiting growth of cells expressing NY-ESO-1 comprising administration of an amount of a recombinant virus according to claims 29 or 91, said amount is effective in inhibiting the growth of the cells.

161. A method of inhibiting the growth of cells expressing NY-ESO-1 comprising administration of an amount of the nucleic acid sequence according to any one of claims 23, 69 or 77, said amount is effective in inhibiting the growth of the cells.

L5 ANSWER 4 OF 15 USPATFULL on STN
2004:285789 Vaccines using high-dose cytokines.
Astsaturov, Igor, Baltimore, MD, UNITED STATES
Petrella, Teresa, North York, CANADA
DeBenedette, Mark, Toronto, CANADA
Berinstein, Neil, Toronto, CANADA
Spaner, David E., Toronto, CANADA
Sunnybrook and Women's College Health Sciences Center Aventis Pasteur, Ltd. (U.S. corporation)
US 2004223949 A1 20041111
APPLICATION: US 2003-690199 A1 20031021 (10)
PRIORITY: US 2002-420425P 20021022 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the field of cancer immunotherapy. In particular, vaccines are administered in conjunction with high doses of cytokines to enhance an anti-tumor immune response.
CLM What is claimed is:
1. A method for treating cancer comprising: a) administering to a host a composition containing a tumor antigen, fragment thereof or nucleic acid encoding the tumor antigen such that the host develops an immune response against the tumor antigen; and, b) subsequently administering to the host a high dose of a **cytokine**; whereby the combination of steps a) and b) provides an enhanced T cell response in the host relative to that which occurs following step a) alone.

2. The method of claim 1 wherein the tumor antigen is administered as a polypeptide or peptide.

3. The method of claim 1 wherein the composition comprises a nucleic acid encoding a tumor antigen.

4. The method of claim 3 wherein the nucleic acid is contained within a plasmid or a viral vector.

5. The method of claim 4 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus.

6. The method of claim 5 wherein the viral vector is a poxvirus selected from the group consisting of vaccinia, NYVAC, MVA, avipox, canarypox, ALVAC, ALVAC(2), **fowlpox**, and **TROVAC**.

7. The method of claim 6 wherein the viral vector is a poxvirus selected from the group consisting of NYVAC, ALVAC, and ALVAC(2).

8. The method of claim 1 wherein the **cytokine** is IFN.

9. The method of claim 8 wherein the **cytokine** is IFN-α.

11. The method of claim 1 wherein the tumor antigen is selected from the group consisting of gp100, MART-1/Melan A, gp75/TRP-1, tyrosinase, NY-ESO-1, melanoma proteoglycan, a MAGE antigen, a BAGE antigen, a GAGE antigen, RAGE antigen, N-acetylglucosaminyltransferase-V, p15, β-catenin, MUM-1, cyclin dependent kinase-4, p21 -ras, BCR-abl, p53, p185 HER2/neu, epidermal growth factor receptor, carcinoembryonic antigen, modified carcinoembryonic antigen, carcinoma-associated mutated mucins, an Epstein Barr Virus EBNA gene product, papilloma virus E7, papilloma virus E6, prostate specific antigen, prostate specific membrane antigen, KSA, kinesin 2, HIP-55, TGFβ-1 anti-apoptotic factor, tumor protein D52, H1FT, an NY-BR antigen, fragments thereof, and derivatives thereof.

12. The method of claim 11 wherein the tumor antigen is selected from the group consisting of gp100, MAGE-1, MAGE-2, MAGE-3, MAGE-4, MAGE-6, MAGE-12, MAGE-51, GAGE-1, GAGE-2, RAGE-1, NY-BR-1, NY-BR-62, NY-BR-75, NY-BR-85, NY-BRP-87, and NY-BR-96.

13. The method of claim 12 wherein the tumor antigen is gp100.

14. The method of claim 1 wherein the composition comprises an poxviral vector encoding a tumor antigen or a fragment thereof and the **cytokine** is a T cell activating **cytokine**.

15. The method of claim 14 wherein poxviral vector is an ALVAC vector and the T cell activating **cytokine** is IFN.

16. The method of claim 15 wherein the T cell activating **cytokine** is IFNα.

17. The method of claim 16 wherein the T cell activating **cytokine** is IFNα2b.

18. The method of claim 17 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least two times per week for at least two weeks.

19. The method of claim 18 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least three times per week for at least two weeks.

20. The method of claim 19 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least four times per week for at least two weeks.

21. The method of claim 20 wherein IFNα2b is administered at at least 10 MU/$m^{2/d}$ IV at least five times per week for at least two weeks.

22. The method of claim 21 wherein IFNα2b is administered at at least 20 MU/$m^{2/d}$ IV at least five times per week for at least four weeks.

L5 ANSWER 5 OF 15 USPATFULL on STN
2004:120585 Recombinant non-replicating virus expressing gm-csf and uses thereof to enhance immune responses.
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US 2004091995 A1 20040513
APPLICATION: US 2003-297168 A1 20030716 (10)
WO 2001-US19201 20010615
DOCUMENT TYPE: Utility; APPLICATION.

AB Replication-defective recombinant poxvirus encoding granulocyte-macrophage colony-stimulating factor (GM-CSF) are disclosed for use in enriching an immunization site with antigen-presenting cells (APC), for enhancing an immunological response to antigen or immunological epitopes by functioning as a biological adjuvant, for prevention or treatment of neutropenia, and for the treatment of myeloidysplastic syndromes. Compositions comprising a replication-defective recombinant virus encoding GM-CSF alone or in combination with a recombinant virus encoding an antigen and optionally encoding an immunostimulatory molecule are disclosed for enhancing antigen-specific immunological responses, in particular enhancing tumor antigen responses for anti-tumor therapy. Methods for enriching an immunization site with APC and for enhancing immunological responses to an antigen or immunological epitope using replication-defective recombinant poxvirus encoding GM-CSF

recombinant avian poxvirus encoding GM-CSF over the use of recombinant GM-CSF is described.

CLM What is claimed is:

1. A pharmaceutical composition comprising a replication-defective virus encoding granulocyte-monocyte-colony stimulating factor (GM-CSF) and a pharmaceutically acceptable carrier.

2. The pharmaceutical composition according to claim 1, wherein the replication-defective virus encodes human GM-CSF.

3. The pharmaceutical composition according to claim 1, wherein the virus is produced using a plasmid vector designated pT5052 deposited with the American Type Culture Collection under Accession No. PTA-2099.

4. The pharmaceutical composition according to claim 1, wherein the replication-defective virus is a poxvirus.

5. The pharmaceutical composition according to claim 1 wherein the replication-defective virus is an avipox virus.

6. The pharmaceutical composition according to claim 5 wherein the avipox virus is selected from the group consisting of **fowlpox** virus, canarypox virus, MVA, and derivatives thereof.

7. The pharmaceutical composition according to any one of claims 1-6, wherein the replication-defective virus further encodes at least one antigen or immunological epitope thereof.

8. The pharmaceutical composition according to claim 7, wherein the antigen is selected from the group consisting of tumor specific antigen, tumor associated antigen, tissue-specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, parasite antigen and mitogen.

9. The pharmaceutical composition according to claim 7, wherein the immunological epitope comprises at least one amino acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 36 and combinations thereof.

10. The pharmaceutical composition according to claim 1 further comprising a vector encoding at least one costimulatory molecule.

11. The pharmaceutical composition according to claim 10, wherein the costimulatory molecule is B7.1.

12. The pharmaceutical composition according to claim 10, wherein the costimulatory molecule is B7.1/ULA-3/ICAM-1.

13. The pharmaceutical composition according to any one of claims 1-12, further comprising a vector encoding alpha **interferon**, beta **interferon**, or gamma **interferon**.

14. The pharmaceutical composition according to any one of claims 1-12 further comprising a vector encoding at least one **cytokine**.

15. The pharmaceutical composition according to claim 14, wherein the **cytokine** is IL-12.

16. The pharmaceutical composition according to any one of claims 1-6, further comprising an Fc receptor-directed bispecific antibody.

17. The pharmaceutical composition according to claim 16, wherein the Fc receptor is selected from the group consisting of FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16).

18. The pharmaceutical composition according to claim 16, wherein the antibody is an anti-CD3-directed antibody.

19. The pharmaceutical composition according to any one of claims 16-18, wherein the bispecific antibody has tumor-directed specificity.

20. The pharmaceutical composition according to claim 19, wherein the specificity is selected from the group consisting of HER-2/neu, EGF-receptor, CD15 antigen and a EpCAM molecule.

21. The pharmaceutical composition according to claims 1-16, further comprising at least one antigen or immunological epitope source, and optionally a conventional adjuvant.

22. The pharmaceutical composition according to claim 21, wherein the conventional adjuvant is selected from the group consisting of Ribi Detox.TM., alum, QS-21, Freund's complete adjuvant, and Freund's

23. The pharmaceutical composition according to claim 21, wherein the antigen or immunological epitope source is a protein, peptide, antibody, anti-idiotypic antibody, lipid, carbohydrate, cell, cell extract, cell fragment, DNA encoding an antigen, or encoding an immunological epitope thereof RNA encoding an antigen or encoding an immunological epitope thereof, or a vector encoding at least one antigen or immunological epitope thereof.

24. The composition according to claim 21, wherein the antigen is selected from the group consisting of a tumor specific antigen, tumor associated antigen, tissue-specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, parasite antigen and mitogen.

25. The composition according to claim 21, wherein the immunological epitope comprises at least one amino acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 36, and combinations thereof.

26. The composition according to claim 24, wherein the bacterial antigen is derived from a bacterium selected from the group consisting of Chlamydia, Mycobacteria, Legionella, Meningiococcus, Group A Streptococcus, Hemophilus influenzae, Salmonella, and Listeria

27. The composition according to claim 24, wherein the viral antigen is derived from a virus selected from the group consisting of Lentivirus, retrovirus, Herpes virus, Hepatitis virus, Orthomyxovirus and Papillomavirus.

28. The composition according to claim 27, wherein the Lentivirus is HIV-1 or HIV-2.

29. The composition according to claim 27, wherein the Herpes virus is HSV or CMV.

30. The composition according to claim 27, wherein the Hepatitis virus is Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D or Hepatitis E.

31. The composition according to claim 27, wherein the orthomyxovirus is influenza virus.

32. The composition according to claim 24, wherein the tumor associated antigen, tumor specific antigen or tissue-specific antigen is selected from the group consisting of CEA, MART-1, MAGE-1, MAGE-3, GP-100, MUC-1, MUC-2, point mutated ras oncogene, normal or point mutated p53, overexpressed p53, CA-125, PSA, PSMA, C-erb/132, BRCA I, BRCA II, PSMA, tyrosinase, TRP-1, TRP-2, NY-ESO-1, TAG72, KSA, HER-2/neu, bcr-abl, pax3-fkhr, ews-fli-1, modified TAAs, splice variants of TAAs, functional epitopes and epitope agonists thereof.

33. The composition according to claim 24, wherein the yeast or fungal antigen is derived from a yeast or fungus selected from the group consisting of Aspergillus, Nocardia, Histoplasmosis, Candida, and Cryptosporidia.

34. The composition according to claim 24, wherein the parasitic antigen is derived from a Plasmodium species, Toxoplasma gondii, Pneumocystis carinii, Trypasosoma species, or Leishmania species.

35. The composition according to claim 23, wherein the vector encoding an antigen or immunological epitope thereof is selected from the group consisting of poxvirus, adenovirus, Herpes virus, alphavirus, picomavirus, iridovirus, DNA plasmids, and RNA.

36. The composition according to claim 35, wherein the poxvirus is orthopox, avipox, capripox or suipox.

37. The composition according to claim 35, wherein the antigen is selected from the group consisting of a tumor specific antigen, tumor associated antigen, tissue-specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, parasite antigen, and mitogen.

38. The composition according to claim 35, wherein the immunological epitope comprises at least one amino acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 36, and combinations thereof.

39. The composition according to claim 23, wherein the antigen or immunological epitope source is a vector encoding at least one antigen or antigenic epitope thereof.

40. The composition according to claim 23, wherein the vector encodes at least one costimulatory molecule selected from the group consisting of B7-1, B7-2, ICAM-1, LFA-3, 4-1BBL, CD59, CD40, CD70, OX-40L, VCAM-1, mammalian homologs thereof and combinations thereof.

41. The composition according to claim 40, wherein the costimulatory molecule is B7.1.

42. The compositon according to claim 40, wherein the costimulatory molecules are at least B7-1, ICAM-1 and LFA-3.

43. The composition according to claim 40, wherein the recombinant replication-defective virus encoding GM-CSF is avipox, the antigen source is a vector encoding CEA or epitope thereof, and the costimulatory molecule is B7 or B7.1/LFA-3/ICAM-1.

44. The composition according to any one of claims 1-15, further comprising a **cytokine**, chemokine or Flt-3L.

45. The composition according to any one of claims 1-15, further comprising at least one antibiotic, antifungal agent, anti-viral agent or combinations thereof.

46. The composition according to any one of claims 1-6, further comprising erythropoietin.

47. The composition according to claim 46, wherein the erythropoietin is recombinantly produced.

48. A host cell infected, transfected or induced with the recombinant replication-defective virus encoding GM-CSF according to any of claims 1-15 and 21-47.

49. The host cell according to claim 48, wherein the host cell is an antigen presenting cell or precursor thereof, a premalignant cell, a hyperplastic cell, tumor cell, or a tumor cell fused to an antigen presenting cell.

50. The host cell according to claim 49, wherein the antigen presenting cell is a dendritic cell or precursor or derivative thereof, a monocyte, macrophage, B-cell, fibroblast or muscle cell.

51. The host cell according to any one of claims 49 or 50, wherein the antigen presenting cell is derived from bone marrow, spleen, skin, peripheral blood, tumor, lymph node, or muscle.

52. The host cell according to claim 50, wherein the derivative is a TNF α-treated dendritic cell, a CD40-treated dendritic cell, or a subpopulation of adherent cells.

53. A dendritic cell or precursor thereof comprising a foreign nucleic acid sequence encoding GM-CSF provided by a recombinant replication-defective virus.

54. A tumor cell or precursor thereof comprising a foreign nucleic acid sequence encoding GM-CSF provided by a recombinant replication-defective virus.

55. The cell according to claims 53 or 54, wherein the cell further comprises a foreign nucleic acid sequence encoding at least one costimulatory molecule.

56. The cell according to claim 55, wherein the costimulatory molecules are selected from the group consisting of B7-1, B7-2, ICAM-1, LFA-3, 4-1BBL, CD59, CD40, CD70, OX-40L, VCAM-1, mammalian homologs thereof and combinations thereof.

57. The cells according to claims 56, wherein the costimulatory molecule is B7.1.

58. The cells according to claim 56, wherein the multiple costimulatory molecules are at least B7-1, ICAM-1 and LFA-3.

59. The cells according to any one of claims 53-58 further comprising a foreign nucleic acid sequence encoding at least one target antigen or immunological epitope thereof.

60. The cells according to claim 59, wherein the foreign nucleic acid sequence encoding at least one target antigen or immunological epitope thereof is provided by a recombinant vector, RNA or DNA from a tumor cell lysate, or by fusion with a tumor cell comprising said sequence.

target antigen or immunological epitope thereof is selected from the group consisting of a tumor specific antigen, tumor associated antigen, tissue-specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, parasite antigen and mitogen.

62. The cells according to any one of claims 59 or 60, wherein the immunological epitope comprises at least one amino acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 36, and combinations thereof.

63. A pharmaceutical composition comprising the cells according to any one of claims 53-62, and optionally an exogenous source of target antigen or immunological epitope thereof.

64. A method of enhancing an immune response in an individual comprising administration of the composition according to any one of claims 1-15 and 21-47 in an amount sufficient to enhance the immune response.

65. The method according to claim 64, wherein a route of administration is intravenous, subcutaneous, intralymphatic, intratumoral, intradermal, intramuscular, intraperitoneal, intrarectal, intravaginal, intranasal, oral, via bladder instillation, intranasal, intraarterial, intravesical or via scarification.

66. The method according to claim 64, wherein the enhancement is migration of antigen presenting cells at an injection site, regional lymph node at a tumor site or combination thereof.

67. The method according to claim 66, wherein the antigen presenting cells express CD11c+/I-Ab+, MHC Class II, or combination thereof.

68. The method according to claim 66, wherein the enhancement is of antigen presenting cell proliferation, function or combination thereof.

69. The method according to claim 64, wherein the enhanced immune response is a cell mediated or humoral response.

70. The method according to claim 64, wherein the enhancement is of CD4+ T cell activation, CD8+ T cell activation, or combination thereof.

71. The method according to claim 64; wherein the enhancement is in IL-2 production, IFN-γ production, TNF-α production, or combinations thereof.

72. A method of enhancing an antigen-specific T-cell response in an individual to a target antigen or immunological epitope thereof comprising administering a recombinant replication-defective poxvirus encoding GM-CSF in combination with a recombinant virus comprising a nucleic acid sequence encoding a target antigen or immunological epitope thereof and optionally also comprising a foreign nucleic acid sequence encoding at least one B7 molecule, a foreign nucleic acid sequence encoding ICAM-1, and a nucleic acid sequence encoding LFA-3, in an amount effective to enhance at least one T-cell response.

73. The method according to claim 72, wherein the enhancement is of CD4+ T cell activation, CD8+ T cell activation, or combination thereof.

74. The method according to claim 72, wherein the enhancement is in IL2 production, IFN-γ production or combination thereof.

75. The method according to claim 72, wherein the enhancement is of antigen-specific cytotoxicity.

76. A method of enhancing an anti-tumor response in an individual with a tumor comprising administration of the composition according to claims 1-15 or 21-47 in an amount effective to enhance the anti-tumor response.

77. The method according to claim 76, further comprising administration of a target antigen or immunological epitope thereof, cell expressing a target antigen or immunological epitope thereof, or cells pulsed with a target antigen or immunological epitope thereof.

78. The method according to any one of claim 76 or 77, wherein the composition is directly injected in situ into a tumor or adjacent to a tumor.

79. The method according to claim 78, wherein the tumor is a head tumor, neck tumor, melanoma, breast tumor, pancreatic tumor, prostate tumor,

80. The method according to claim 79, wherein the tumor is a metastatic breast skin lesion.

81. The method according to any one of claims 76-79, wherein the composition is injected during surgery.

82. The method according to claim 81, wherein the tumor is a colonrectal cancer or pancreatic cancer.

83. The method according to any one of claims 76-79, wherein the composition is injected into a lymph node distal to or draining a tumor site.

84. The method according to any one of claims 76-79, further comprising the administration of activated, target antigen specific lymphocytes.

85. The method according to any one of claims 76-79, wherein the anti-tumor response is tumor regression, increase in disease-free interval, or increase in survival.

86. A method of enhancing an immune response in an individual comprising administration of a cell according to any of claims 48-62 in an amount effective to enhance an immune response.

87. A method of enhancing an immune response in an individual comprising administration of a tumor cell, or precursors thereof according to claim 49 or 54 in an amount effective to enhance an immune response.

88. The method according to any one of claims 86 or 87, wherein the cells are autologous, syngeneic or allogeneic with the individual.

89. The method according to any one of claims 86 or 87, wherein the cells have been pulsed with a target antigen or epitope thereof.

90. The method according to any one of claims 86 or 87, further comprising the administration of a target cell, target antigen or immunological epitope thereof.

91. The method according to any one of claims 86-90, further comprising the administration of activated, target antigen specific lymphocytes.

92. A method of enhancing an immune response to an antigen or immunological epitope thereof in an individual comprising administration of a first recombinant vector encoding GM-CSF followed by administration of a second recombinant vector encoding GM-CSF wherein at least one recombinant vector is a replication-defective virus.

93. The method according to claim 92, wherein the replication defective virus is selected from the group consisting of poxvirus, herpes virus, adenovirus and adeno-associated virus.

94. The method according to claim 93, wherein the poxvirus is selected from the group consisting of **fowlpox**, canary pox and a Modified Vaccinia Ankara strain.

95. The method according to claim 92, wherein a second recombinant vector is replication competent.

96. The method according to claim 95, wherein the second vector is vaccinia.

97. A method of treating neutropenia in an individual comprising administration of a recombinant replication-defective virus encoding GM-CSF in an amount effective to treat the neutropenia.

98. The method according to claim 97, further comprising the administration of an antibiotic, antifungal agent, antiparasite agent, or antiviral agent.

99. The method according to claim 97, wherein the neutropenia is resultant from chemotherapy, corticosteroid therapy, irradiation, or an infection.

100. The method according to any one of claims 97-99, wherein a dose raises the neutrophil count to normal levels.

101. A method for treating cytopenias in patients with myeloidysplastic syndrome comprising administration of a recombinant replication-defective virus encoding GM-CSF in combination with erythropoietin in an amount effective to treat the cytopenia.

about 10^5 to about 10^{10} pfu of the recombinant replication-defective virus encoding GM-CSF is administered at a weekly or monthly interval.

103. The method according to any one of claims 101 or 102, wherein a dose in the range of about 150 to about 300 u/k of erythropoietin is administered.

104. The method according to any one of claims 101-104, wherein the dose is provided on alternate days.

105. The method according to any one of claims 101-104, wherein the treatment increases the neutrophil count and erythroid precursors.

106. A method of enhancing an antitumor immune response comprising administration of a replication-defective virus encoding GM-CSF in combination with a bispecific antibody.

107. The method according to claim 106, wherein the bispecific antibody has tumor-directed specificity.

108. The method according to claim 107, wherein the bispecific antibody has a specificity selected from the group consisting of HER-2/neu, EGF-receptor, CD15 antigen and a EpCAM molecule.

109. The method according to any one of claims 107-108, wherein the bispecific antibody is directed to a tumor cell epitope and a cytotoxin trigger molecule.

110. A method of enhancing an immune response to a vaccination comprising administration of a replication-defective virus encoding GM-CSF at the vaccination site or regional lymph node in an amount effective to enhance the immune response to a vaccine.

111. The method according to claim 110, wherein the vaccine comprises at least one tumor antigen or tumor associated antigen.

112. The method according to claim 110, wherein the vaccine is selected from the group consisting of DPT vaccine, Td vaccine, DtaP vaccine, Hib vaccine, DtaP-Hib vaccine, MMR vaccine, Hepatitis A vaccine, Hepatitis B vaccine, Lyme's disease vaccine, influenza vaccine, tetravalent meningococcal polysaccharide, pneumococcal polysaccharide vaccine, anthrax vaccine, cholera vaccine, plague vaccine, yellow fever vaccine and Bacillus Calmette-Guerin vaccine.

113. An immunological adjuvant comprising a replication-defective virus encoding granulocyte-monocyte-colony stimulating factor.

114. A plasmid vector encoding human granulocyte-monocyte colony stimulating factor deposited with the American Type Culture Collection under Accession No. PTA-2099.

L5 ANSWER 6 OF 15 USPATFULL on STN
2004:76663 Avian cell lines useful for the production of substances of interest

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PRIORITY: WO 2003-FR735 20030307
FR 2002-2945 20020308
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a method for producing avian cell lines, comprising gradual or complete withdrawal of growth factors, serum and/or feeder layer so that the established lines are adherent or nonadherent cells capable of proliferating indefinitely in a basic culture medium. The invention also relates to the cells derived from such lines which are particularly useful for the production of substances of interest.
CLM What is claimed is:
1. A method for producing avian cell lines, wherein it comprises the following steps: a) culturing avian cells in a medium containing all the factors allowing their growth and an inactivated feeder layer, b) passage by modifying the culture medium so as to obtain progressive or total withdrawal of said factors, of the serum and/or of the feeder layer, c) establishing adherent or nonadherent cell lines capable of proliferating in a basal medium in the absence of exogenous growth factors, serum and/or inactivated feeder layer.

cell lines obtained in step c) are capable of proliferating for at least 50 days, preferably at least 600 days.

3. The method according to claim 1, wherein step b) consists in a progressive or total withdrawal of the feeder layer, optionally followed by a progressive withdrawal of the growth factors and/or the serum.

4. The method according to claim 1, wherein step b) consists in a progressive or total withdrawal of the growth factors, optionally followed by a progressive withdrawal of the serum.

5. The method according to claim 1, wherein step b) consists in a progressive or total withdrawal of the growth factors and/or serum, optionally followed by a withdrawal of the feeder layer.

6. The method according to claim 1, wherein the cells obtained in step c) are subjected to a selection in culture media used for large-scale production so as to obtain clones suitable for the production of vaccine intended for human or animal therapy.

7. The method according to claim 1, wherein the cells derived from the lines obtained in step c) are avian stem cells.

8. The method according to claims 7, wherein the cells derived from the lines obtained in step c) are avian embryonic stem cells.

9. The method according to claim 7, wherein the cells derived from the lines obtained in step c) are avian somatic stem cells.

10. The method according to claim 1, wherein the cells derived from the lines obtained in step c) are adherent stem cells which proliferate in the absence of the inactivated feeder layer.

11. The method according to claim 1, wherein the cells derived from the lines obtained in step c) are nonadherent stem cells which proliferate in suspension in a medium free of exogenous growth factors.

12. The method according to claim 9, wherein the avian somatic stem cells are nonadherent cells which proliferate in suspension in a medium free of exogenous growth factors.

13. The method according to claim 1, wherein the cells derived from the lines obtained in step c) proliferate in a medium free of serum.

14. The method according to claim 9, wherein the avian somatic stem cells are nonadherent cells which proliferate in suspension in a medium free of serum.

15. The method according to claim 1, wherein the cells derived from the lines obtained in step c) have at least one of the following characteristics: a high nucleocytoplasmic ratio, an endogenous alkaline phosphatase activity, an endogenous telomerase activity, a reactivity with specific antibodies selected from the group of antibodies SSEA-1 (TEC01), SSEA-3, and EMA-1.

16. The method according to claim 1, wherein the cells derived from the lines obtained in step c) are modified in order to allow a better use in vitro such as the extension of the greater life span or growth densities or alternatively of the lower nutrient requirements.

17. The method according to claim 1, wherein the cells derived from the lines obtained in step c) are modified in order to produce a substance of interest, in particular a polypeptide of interest, an antibody or an attenuated virus.

18. The method according to claim 1, wherein the medium used in step a) comprises at least one factor selected from cytokines, in particular LIF, IL-11, IL-6, IL-6R, CNTF, Oncostatin and other factors such as SCF, IGF-1 and bFGF.

19. The method according to claim 1, wherein the inactivated feeder layer used in step a) is composed of fibroblast cells including mouse fibroblasts established as a line, in particular transformed or nontransformed STO cells.

20. The method according to claim 1, wherein the cells used in step a) are cells obtained by suspending cells obtained from blastodermal disks of fertilized eggs in a culture medium comprising at least one **cytokine**, b-FGF, and SCF, said cells being inoculated into a layer of feeder cells, incubated, and then collected.

21. The method according to claim 1, wherein step b) comprises a

a), in particular a **cytokine**, b-FGF, and SCF, comprising a passage in a new medium free of at least one of said factors and in repeating various successive passages until the medium is free of all of said factors.

22. The method according to claim 21, wherein step b) additionally comprises the withdrawal of the serum.

23. The method according to claim 21, wherein step b) additionally comprises the withdrawal of the feeder layer.

24. The method according to claim 1, wherein step b) comprises a progressive withdrawal of the serum, comprising successive passages in new media comprising decreased serum concentration and in repeating various successive passages until the medium is free of serum.

25. The method according to claim 1, wherein step b) comprises the withdrawal of the feeder layer, said withdrawal being either progressive comprising successive passages in new media comprising decreased feeder cells number and in repeating various successive passages until the medium is free of feeder cells.

26. A cell line and cell derived thereof which can be obtained from the method according to claim 1, wherein it is capable of proliferating for at least 50 days, preferably at least 600 days in a medium free of exogenous growth factor.

27. A cell line and cells derived thereof which can be obtained from the method according to claim 1, wherein it is capable of proliferating for at least 50 days, preferably at least 600 days in a medium depleted of serum and in particular free of serum.

28. A cell line and cells derived thereof which can be obtained from the method according to claim 1, wherein it is capable of proliferating for at least 50 days, preferably at least 600 days in a medium free of feeder layer.

29. A cell line and cells derived thereof which can be obtained from the method according to claim 1, wherein it is capable of proliferating for at least 50 days, preferably at least 600 days in a medium free of exogenous growth factor, depleted of serum or free of serum and/or of feeder layer.

30. A cell line and cells derived thereof which can be obtained from the method according to claim 9, wherein it is capable of proliferating for at least 50 days, preferably at least 600 days in a medium free of exogenous growth factor, depleted of serum or free of serum and/or of feeder layer.

31. The cell line and cells derived thereof according to claims 29 or 30, wherein it is capable of proliferating for at least 50 days, preferably at least 600 days in a basal medium, in particular in a medium such as DMEM, GMEM, HamF12 or McCoy supplemented with various additives such as nonessential amino acids, vitamins and sodium pyruvate.

32. The cell line and cells derived thereof according to claim 26, wherein it is an avian stem cell.

33. The cell line and cell derived from such a line according to claim 32, wherein it is an avian embryonic stem cell.

34. The cell line and cells derived thereof according to claim 32, wherein it is an avian somatic stem cell.

35. The cell line and cells derived thereof according to claim 32, wherein it is an adherent stem cell which proliferates in the absence of the inactivated feeder layer.

36. The cell line and cells derived thereof according to claim 32, wherein it is a nonadherent stem cell which proliferates in suspension.

37. The cell line and cells derived thereof according to one of claim 32, wherein it has at least one of the following characteristics: a high nucleocytoplasmic ratio, an endogenous alkaline phosphatase activity, an endogenous telomerase activity, a reactivity with specific antibodies selected from the group of antibodies SSEA-1 (TEC01), SSEA-3, and EMA-1.

38. The cell line and cells derived thereof according to one of claims 32, wherein they are genetically modified so as to produce a substance of interest, in particular a polypeptide of interest, an antibody or an

39. The cell line and cells derived thereof according to claim 38, wherein they support the replication of live or attenuated viruses, in particular the viruses selected from the group of adenoviruses, hepadnaviruses, herpesviruses, orthomyxoviruses, papovaviruses, paramyxoviruses, picornaviruses, poxviruses, reoviruses and retroviruses.

40. The cell line and cells derived thereof according to claim 39, wherein the viruses replicated on these cells belong to the family of orthomyxoviruses, in particular the influenza virus.

41. The cell line and cells derived thereof according to claim 39, wherein the replicated viruses belong to the family of paramyxoviruses, in particular the measles, mumps and rubella viruses.

42. The cell line and cells derived thereof according to claim 39, wherein the replicated viruses belong to the group of poxviruses such as attenuated vaccinia virus and in particular Avipox virus such as canarypox virus, **Fowlpox** virus, Juncopox virus, Mynahpox virus, Pigeonpox virus, Psittacinepox virus, Quailpox virus, Sparrowpox virus, Starlingpox virus and Turkeypox virus.

43. A cell line derived from step c) of the method according to one of claims 1, wherein it is a genetically modified avian stem cell capable of growing indefinitely in a basal medium free of exogenous growth factors, depleted of serum and/or free of serum and/or of feeder layer.

44. The use of the cell line and cells derived thereof according to claim 32 for the production of substances of interest, in particular of proteins of therapeutic interest.

45. The use of the cell line and cells derived thereof according to claim 32, for the replication of live or attenuated viruses, in particular viruses chosen from the group of adenoviruses, hepadnaviruses, herpesviruses, orthomyxoviruses, papovaviruses, paramyxoviruses, picornaviruses, poxviruses such as vaccinia virus and in particular Avipox virus in particular canarypox virus, **Fowlpox** virus, Juncopox virus, Mynahpox virus, Pigeonpox virus, Psittacinepox virus, Quailpox virus, Sparrowpox virus, Starlingpox virus and Turkeypox virus, as well as reoviruses and retroviruses.

46. The use of the line according to claim 32, for the production of viruses belonging to the family of orthomyxoviruses, in particular the influenza virus.

47. The use of the line according to claim 32 for the production of viruses belonging to the family of paramyxoviruses, in particular the measles, mumps and rubella viruses.

48. The use of the line according to claim 39, for supporting the replication of live or attenuated viruses, in particular by introducing the component(s) necessary for accomplishing the complete viral cycle of the virus in the cell, in particular the overexpression of the receptor for the virus at the surface of the cell.

49. The use according to claim 39, for supporting the replication of live or attenuated viruses, in particular by introducing the component(s) necessary for accomplishing the complete viral cycle of the virus in the cell, in particular the overexpression of the receptor for the virus at the surface of the cell, said viruses being selected from the group of poxviruses such as vaccinia virus (for example Modified vaccinia virus Ankara, MVA) and in particular Avipox virus such as canarypox virus, **Fowlpox** virus, Juncopox virus, Mynahpox virus, Pigeonpox virus, Psittacinepox virus, Quailpox virus, Sparrowpox virus, Starlingpox virus and Turkeypox virus.

50. The use according to claim 39 to produce live or attenuated vaccine comprising culturing the adherent or non adherent cell lines established in step c) according to the process described above, inoculating said cells with viral particles and culturing said cells in a basal medium as mentioned above until cell lysis occurs and newly produced viral particles are released in said medium.

51. The use according to claim 39 to produce live or attenuated, native or recombinant, vaccine selected from the group consisting of the family of adenoviruses (such as Human Adenovirus C, Fowl Adenovirus A, Ovine Adenovirus D, Turkey Adenovirus B), circoviridae (such as Chicken Anemia Virus, CAV), coronaviruses, such as avian infectious bronchitis virus (IBV), flaviviruses (such as Yellow fever virus and hepatitis C virus), hepadnaviruses (such as Hepatitis B virus and Avihepadnaviruses such as Duck hepatitis B virus); herpesviruses (such as Gallid herpesvirus, HSV

orthomyxoviruses (such as the influenza virus: Influenzavirus A, Influenzavirus B and Influenza-virus C), papovaviruses (such as polyomavirus and more particularly Simian virus 40), paramyxoviruses (such as measles, mumps and rubella viruses and such as respiroviruses and pneumoviruses such as human respiratory syncytial virus and Metapneumovirus such as Avian pneumovirus), picornaviruses (such as polio virus, hepatitis A virus, and such as Encephalomyocarditis virus and foot-and-mouth disease virus), poxviruses (such as **fowlpox** virus and avipox viruses including Canarypox viruses, Juncopox viruses, Mynahpox viruses, Pigeonpox viruses, Psittacinepox viruses, Quailpox viruses, Sparrowpox viruses, Starlingpox viruses, Turkeypox viruses), orthopoxvirus such as vaccinia virus, MVA, and reoviruses (such as rotaviruses), retroviruses (such as ALV, avian leukosis virus, Gammaretroviruses such as Murine leukemia virus, Lentiviruses such as Human immunodeficiency virus 1 and 2) and Togaviridae such as Rubivirus, in particular Rubella virus.

52. The use according claim 45 to produce a vaccine against smallpox.

53. The use according claim 45 to produce a recombinant vaccine against cancer.

L5 ANSWER 7 OF 15 USPATFULL on STN
2004:25353 Recombinant vector expressing multiple costimulatory molecules and uses thereof.
Scholm, Jeffrey, Potomac, MD, UNITED STATES
Hodge, James, Gaithersburg, MD, UNITED STATES
Panicali, Dennis, Acton, MA, UNITED STATES
US 2004019195 A1 20040129
APPLICATION: US 2003-406317 A1 20030404 (10)
PRIORITY: US 1998-111582P 19981209 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is a recombinant vector encoding and expressing at least three or more costimulatory molecules. The recombinant vector may additionally contain a gene encoding one or more target antigens or immunological epitope thereof. The synergistic effect of these costimulatory molecules on the enhanced activation of T cells is demonstrated. The degree of T-cell activation using recombinant vectors containing genes encoding three costimulatory molecules was far greater than the sum of recombinant vector constructs containing one costimulatory molecule and greater than the use of two costimulatory molecules. Results employing the triple costimulatory vectors were most dramatic under conditions of either low levels of first signal or low stimulator to T-cell ratios. This phenomenon was observed with both isolated CD4+ and CD8+ T cells. The recombinant vectors of the present invention are useful as immunogenes and vaccines against cancer and pathogenic micro-organisms, and in providing host cells, including dendritic cells and splenocytes with enhanced antigen-presenting functions.

CLM What is claimed is:
1. A recombinant vector comprising foreign nucleic acid sequences encoding multiple costimulatory molecules or functional portions thereof.

2. The recombinant vector according to claim 1 wherein the nucleic acid sequences encode at least three costimulatory molecules.

3. The recombinant vector according to claim 1 wherein the nucleic acid sequence encoding each costimulatory molecule is derived from a mammalian source.

4. The recombinant vector according to claim 1 wherein the multiple costimulatory molecules are selected from the group consisting of B7-1, B7-2, ICAM-1, LFA-3, 4-1BBL, CD59, CD40, CD70, OX-40L, VCAM-1 and mammalian homologs thereof.

5. The recombinant vector according to claim 5 wherein the multiple costimulatory molecules are B7-1, ICAM-1 and LFA-3.

6. The recombinant vector according to claim 1 further comprising a foreign nucleic acid sequence encoding at least one **cytokine**, chemokine, Flt-3L, or combination thereof.

7. The recombinant vector according to claim 1 further comprising a multiplicity of promoters.

8. The recombinant vector according to claim 7 wherein the promoters are derived from a eukaryotic source, prokaryotic source, or viral source.

9. The recombinant vector according to claim 7 wherein the promoters are

promoter, adenovirus major late promoter, human CMV immediate early I promoter, poxvirus promoter, 30K promoter, I3 promoter, sE/L promoter, 7.5K promoter, 40K promoter, and C1 promoter.

10. The recombinant vector according to claim 1 wherein the recombinant vector is selected from the group consisting of a bacteria, virus, and nucleic acid-based vector.

11. The recombinant vector according to claim 1 wherein the recombinant vector is selected from the group consisting of poxvirus, adenovirus, Herpes virus, alphavirus, retrovirus, picornavirus, and iridovirus.

12. The recombinant vector according to claim 11 wherein the recombinant vector is a recombinant poxvirus.

13. The recombinant vector according to claim 12 wherein the recombinant poxvirus is a replicating virus or a non-replicating virus.

14. The recombinant vector according to claim 12 wherein the recombinant poxvirus is orthopox, avipox, capripox or suipox.

15. The recombinant vector according to claim 14 wherein the avipox is **fowlpox**, canary pox or derivatives thereof.

16. The recombinant vector according to claim 14 wherein the orthopox is vaccinia, vaccinia-Copenhagen strain, vaccinia-Wyeth strain, NYVAC, vaccinia-MVA strain, raccoon pox or rabbit pox.

17. The recombinant vector according to claim 1 further comprising a foreign nucleic acid sequence encoding at least one target antigen or immunological epitope thereof.

18. The recombinant vector according to claim 17 wherein the target antigen has an amino acid sequence selected from the group consisting of SEQ ID NO: 2 through SEQ ID NO: 40.

19. The recombinant vector according to claim 17 wherein the target antigen is selected from the group consisting of a tumor specific antigen, tumor associated antigen, tissue-specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, and parasite antigen and mitogen.

20. The recombinant vector according to claim 18 wherein the bacterial antigen is derived from a bacterium selected from the group consisting of Chiamydia, Mycobacteria. Legionella, Meningiococcus, Group A Streptococcus, Hemophilus influenzae, Salmonella, and Listeria.

21. The recombinant vector according to claim 18 wherein the viral antigen is derived from a virus selected from the group consisting of Lentivirus, Herpes virus, Hepatitis virus, Orthomyxovirus and Papillomavirus.

22. The recombinant vector according to claim 21 wherein the Lentivirus is HIV-1 or HIV-2.

23. The recombinant vector according to claim 21 wherein the Herpes virus is HSV or CMV.

24. The recombinant vector according to claim 21 wherein the Hepatitis virus is Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D or Hepatitis E.

25. The recombinant vector according to claim 21 wherein the orthomyxovirus is influenza virus.

26. The recombinant vector according to claim 18 wherein the tumor associated antigen, tumor specific antigen or tissue-specific antigen is selected from the group consisting of CEA, MART-1, MAGE-1, MAGE-3, GP-100, MUC-1, MUC-2, pointed mutated ras oncogene, normal or point mutated p53, overexpressed p53, CA-125, PSA, C-erb/B2, BRCA I, BRCA II, PSMA, tyrosinase, TRP-1, TRP-2, NY-ESO-1, TAG72, KSA, HER-2/neu, bcr-abl, pax3-fkhr, ews-fli-1, modified TAAs, splice variants of TAAs, functional epitopes and epitope agonists thereof.

27. The recombinant vector according to claim 26 wherein the antigen is CEA (6D) having an amino acid aspartic acid at amino acid position 576.

28. The recombinant vector according to claim 26 wherein the antigen is PSA and PSMA.

29. The recombinant vector according to claim 26 wherein the antigen is MUC-1 encoded by a truncated MUC-1 gene consisting of a signal sequence,

30. The recombinant vector according to claim 18 wherein the yeast or fungal antigen is derived from a yeast or fungus selected from the group consisting of Aspergillus, Nocardia, Histoplasmosis, Candida, and Cryptosporidia.

31. The recombinant vector according to claim 18 wherein the parasitic antigen is derived from a Plasmodium species, Toxoplasma gondii, Pneumocystis carinii, Trypasosoma species, or Leishmania species.

32. The recombinant vector according to claim 1 wherein the vector further comprises a selectable marker.

33. The recombinant vector according to claim 32 wherein the selectable marker is selected from the group consisting of lacZ gene, thymidine kinase, gpt, GUS and a vaccinia K1L host range gene.

34. A pharmaceutical composition comprising at least one recombinant vector according to any of claims 1-33 and a pharmaceutically acceptable carrier.

35. A pharmaceutical composition comprising at least one recombinant vector according to any of claims 1-16, a second recombinant vector comprising at least one nucleic acid sequence encoding at least one target antigen or immunological epitope thereof and a pharmaceutically acceptable carrier.

36. A pharmaceutical composition according to claim 34 or 35 further comprising a **cytokine**, chemokine or Flt-3L.

37. A host cell infected, transfected or induced with the recombinant vector according to any of claims 1-33.

38. The host cell infected, transfected or induced with the recombinant vector according to claims 1-16 and infected, transfected or induced with a second recombinant vector comprising at least one foreign nucleic acid sequence encoding at least one target antigen or immunological epitope thereof.

39. The host cell according to claim 38 wherein the host cell is an antigen presenting cell or precursor thereof, a premalignant cell, a hyperplastic cell or tumor cell.

40. The host cell according to claim 39 wherein the antigen presenting cell is a dendritic cell or precursor thereof, a monocyte, macrophage, B-cell, fibroblast or muscle cell.

41. The host cell according to claim 39 wherein the antigen presenting cell is derived from bone marrow, spleen, skin, peripheral blood, tumor, lymph node, or muscle.

42. The host cell according to claim 38 wherein the host cell is an antigen presenting cell or precursor thereof, a premalignant cell, a hyperplastic cell or tumor cell.

43. The host cell according to claim 42 wherein the antigen presenting cell is a dendritic cell, precursor or derivative thereof, a monocyte, macrophage, B-cell, fibroblast or muscle cell.

44. The host cell according to claim 43 wherein the derivative is a TNF α-treated dendritic cell, a CD40-treated dendritic cell, or a subpopulation of adherent cells.

45. A dendritic cell or precursor thereof comprising a foreign nucleic acid sequence encoding multiple costimulatory molecules.

46. A tumor cell or precursor thereof comprising a foreign nucleic acid sequence encoding multiple costimulatory molecules.

47. The cell according to claims 45 or 46 wherein the cell comprises a foreign nucleic acid sequence encoding at least three costimulatory molecules.

48. The cell according to claims 45 or 46 wherein the multiple costimulatory molecules are selected from the group consisting of B7-1, B7-2, ICAM-1, LFA-3, 4-1BBL, CD59, CD40, CD70, OX-40L, VCAM-1, mammalian homologs thereof and combinations thereof.

49. The cells according to claims 45 or 46 wherein the multiple costimulatory molecules are at least B7-1, ICAM-1 and LFA-3.

50. The cells according to claims 45 or 46 further comprising a foreign

immunological epitope thereof.

51. The cells according to claim 50 wherein the foreign nucleic acid sequence encoding at least one target antigen or immunological epitope thereof is provided by a recombinant vector, RNA or DNA from a tumor cell lysate, or by fusion with a tumor cell comprising said sequence.

52. The cells according to claim 50 wherein the target antigen or immunological epitope thereof is selected from the group consisting of a tumor specific antigen, tumor associated antigen, tissue-specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, parasite antigen and mitogen.

53. A pharmaceutical composition comprising the cells according to claims 45-52 and optionally an exogenous source of target antigen or immunological epitope thereof.

54. A recombinant poxvirus having integrated into a viral genome foreign DNA encoding multiple costimulatory molecules produced by a process comprising: allowing a plasmid vector comprising the foreign DNA encoding multiple costimulatory molecules to undergo recombination with a parental poxvirus genome to produce a recombinant poxvirus having inserted into its genome the foreign DNA.

55. A recombinant poxvirus having integrated into a viral genome foreign DNA encoding LFA-3, ICAM-1 and at least one B7 molecule produced by a process comprising: allowing a plasmid vector comprising the foreign DNA encoding LFA-3, ICAM-1 and at least one B7 molecule to undergo recombination with a parental poxvirus genome to produce a recombinant poxvirus having inserted into its genome the foreign DNA.

56. The recombinant poxvirus according to claim 54 or 55, wherein the genome further comprises a multiplicity of poxvirus promoters capable of controlling expression of the foreign DNA.

57. The recombinant poxvirus according to claims 54 or 55 further comprising a foreign gene encoding at least one target antigen or immunological epitope thereof.

58. A pharmaceutical composition comprising a recombinant poxvirus according to any of claims 54-57 and a pharmaceutically acceptable carrier.

59. A pharmaceutical composition comprising a recombinant poxvirus according to any of claims 54-57 further comprising a second recombinant poxvirus comprising at least one foreign nucleic acid sequence encoding at least one target antigen or immunological epitope thereof.

60. A host cell infected with the recombinant poxvirus according to claims 54-57.

61. The host cell according to claim 60, wherein the cell is a progenitor antigen presenting cell, an antigen presenting cell or an engineered antigen presenting cell.

62. The host cell according to claim 61, wherein the cell is a progenitor dendritic cell, dendritic cell, monocyte, macrophage, B-cell, fibroblast or muscle cell.

63. The host cell according to claim 60, wherein the cell is a hyperplastic cell, premalignant cell or a tumor cell.

64. A plasmid vector comprising nucleic acid sequences encoding multiple costimulatory molecules or functional portions thereof.

65. The plasmid vector according to claim 64 further comprising a gene encoding a selectable marker.

66. The plasmid vector according to claim 64 wherein the costimulatory molecules are human derived, non-human primate derived or murine derived.

67. The plasmid vector according to claim 64 further comprising a foreign nucleic acid sequence encoding at least one target antigen or immunological epitope thereof.

68. The plasmid vector according to claim 67 wherein the target antigen is selected from the group consisting of a tumor specific antigen, tumor associated antigen, tissue specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, parasite antigen, and mitogen.

is carcinoembryonic antigen (CEA) or immunological epitope thereof.

70. A plasmid vector for recombination with a poxvirus designed to produce a recombinant poxvirus capable of expressing foreign nucleic acid sequences encoding three costimulatory molecules, LFA-3, ICAM-1 and at least one B7 molecule which comprises (a) a multiplicity of poxviral promoters, (b) the foreign nucleic acid sequences encoding LFA-3, ICAM-1 and at least one B7 molecule, (c) DNA sequences flanking the construct of elements (a) and (b), the flanking sequences of both the 5' and 3' ends being homologous to a region of a parental poxvirus genome where elements (a) and (b) are to be inserted.

71. The plasmid vector according to claim 64 designated pT5064 deposited with the ATCC under Accession No. 203482

72. The plasmid vector according to claim 67, designated pT5049 deposited with the ATCC under Accession No. 203481.

73. A kit for use in making a recombinant poxvirus comprising a plasmid vector according to any of claims 64-72 and optionally a parental poxvirus.

74. A method of making a recombinant poxvirus comprising allowing the plasmid vector according to claim 64-72 to undergo recombination with a parental poxvirus genome to produce a recombinant poxvirus having inserted into its genome the foreign DNA and a multiplicity of poxvirus promoters capable of controlling the expression of the foreign DNA.

75. A method of enhancing an immune response in an individual comprising administration of a recombinant vector according to claims 1-33 in an amount sufficient to enhance the immune response.

76. The method according to claim 75 wherein a route of administration is intravenous, subcutaneous, intralymphatic, intratumoral, intradermal, intramuscular, intraperitoneal, intrarectal, intravaginal, intranasal, oral, via bladder instillation, or via scarification.

77. The method according to claim 75 wherein the enhanced immune response is a cell mediated or humoral response.

78. The method according to claim 75, wherein the enhancement is of CD4+ T cell proliferation, CD8+ T cell proliferation, or combination thereof.

79. The method according to claim 75, wherein the enhancement is of CD4+ T cell function, CD8+ T cell function or combination thereof.

80. The method according to claim 75, wherein the enhancement is in IL-2 production, IFN-γ production or combination thereof.

81. The method according to claim 75, wherein the enhancement is of antigen presenting cell proliferation, function or combination thereof.

82. A method of enhancing an antigen-specific T-cell response in an individual to a target antigen or immunological epitope thereof comprising administering a recombinant poxvirus comprising a foreign nucleic acid sequence encoding at least one B7 molecule, a foreign nucleic acid sequence encoding ICAM-1, and a nucleic acid sequence encoding LFA-3, and optionally a nucleic acid sequence encoding a target antigen or immunological epitope thereof, each nucleic acid sequence expressed in an infected cell in the individual in an amount effective to enhance at least one T-cell response, wherein the enhancement is greater than the enhancement obtained using a single costimulatory molecule or two costimulatory molecules.

83. The method according to claim 82, wherein the enhancement is of CD4+ T cell proliferation, CD8+ T cell proliferation, or combination thereof.

84. The method according to claim 82, wherein the enhancement is in IL-2 production, IFN-γ production or combination thereof.

85. The method according to claim 82, wherein the enhancement is of antigen-specific cytotoxicity.

86. The method according to claim 82 wherein the infected cell is an antigen presenting cell.

87. The method according to claim 86, wherein the cell is a dendritic cell, precursor thereof, monocyte, macrophage, B-cell fibroblast or muscle cell.

88. The method according to claim 82, wherein the infected cell is a tumor cell or precursor thereof.

89. A method of treatment or prevention of disease in an individual comprising: (a) activating a T lymphocyte by exposing the T lymphocyte in vitro to a cell according to claim 37 alone or in combination with a target antigen or immunological epitope thereof; (b) administering the activated T lymphocyte to an individual alone, or in combination with the target antigen in an amount sufficient to enhance an immune response.

90. The method according to claim 89 wherein the T lymphocytes are autologous with the individual.

91. The method according to claim 89, further comprising the administration of a **cytokine**, chemokine, flt-31 or combination thereof.

92. The method according to claim 89 wherein the immune response is against the target antigen selected from the group consisting of a tumor specific antigen, tumor associated antigen, tissue-specific antigen, bacterial antigen, viral antigen, yeast antigen, fungal antigen, protozoan antigen, and parasite antigen.

93. The method according to claim 89 wherein the immune response prevents or treats a disease caused by a cell or organism selected from the group consisting of viruses, bacteria, protozoans, parasites, premalignant cells and tumor cells.

94. A method of enhancing an immune response in an individual comprising administration of a cell according to any of claims 45-52 in an amount effective to enhance an immune response.

95. A method of enhancing an immune response in an individual comprising administration of a tumor cell, or precursors thereof according to claim 46 in an amount effective to enhance an immune response.

96. The method according to claims 94 or 95 wherein the cells are autologous, syngeneic or allogeneic with the individual.

97. The method according to claims 94 or 95 wherein the cells have been pulsed with a target antigen or epitope thereof.

98. The method according to claims 94 or 95 further comprising the administration of a target cell, target antigen or immunological epitope thereof.

99. The method according to claim 94 further comprising the administration of activated, target antigen specific lymphocytes.

100. A method for making a progenitor dendritic cell or dendritic cell that overexpresses multiple costimulatory molecules, said method comprising: (a) providing the cell with a recombinant vector comprising foreign genes encoding multiple costimulatory molecules for a period of time sufficient to cause overexpression of the multiple costimulatory molecules by the cells.

101. The method according to claim 100 wherein the cells are isolated from bone marrow or peripheral blood mononuclear cells.

102. The method according to claim 100 wherein the recombinant vector further comprises a foreign gene encoding at least one target antigen or immunological epitope thereof.

103. The method according to claim 100 further comprising (b) providing the cell with a second recombinant vector comprising a foreign gene encoding at least one target antigen or immunological epitope thereof.

104. An in vitro method of assessing efficacy of a vaccine against a target antigen comprising: (a) obtaining lymphocytes from an individual previously vaccinated with a target antigen or epitope thereof, (b) determining the number and function of target-antigen specific lymphocytes in the presence of antigen presenting cells according to claim 39, an increase in number, function or combination thereof of target-antigen specific lymphocytes being indicative of efficacy of the vaccine.

105. A method of screening for novel immunogenic peptides from a multiplicity of peptides comprising: (a) pulsing antigen presenting cells infected with a recombinant vector encoding multiple costimulatory molecules with a multiplicity of peptides to form peptide-pulsed antigen presenting cells; (b) measuring lymphoid immunoreactivity in the presence of the peptide-pulsed antigen presenting cells, wherein

peptide-pulsed antigen presenting cell.

106. The method according to claim 105, wherein the source of the multiplicity of peptides is a combinatorial peptide library.

L5 ANSWER 8 OF 15 USPATFULL on STN
2004:24340 Vacination method.
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Schneider, Joerg, Oxford, UNITED KINGDOM
US 2004018177 A1 20040129
APPLICATION: US 2003-345000 A1 20030715 (10)
WO 2001-GB4116 20010913
PRIORITY: GB 2000-232033 20000921
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There is provided a method of inducing a CD4+ T-cell response against a target antigen, by administering a composition a source of one or more CD4+ epitopes is a non-replicating or replication impaired recombinant poxvirus vector.

CLM What is claimed is:

1. A method of inducing a CD4+ T-cell response against a target antigen, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes of the target antigen; and at least one dose of (b) a second composition comprising a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition, wherein the source of CD4+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector, and wherein the doses of the first and second compositions may be administered in either order.

2. A method inducing a combined CD4+ and CD8+ T-cell response against a target antigen, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes and a source of one or more CD8+ T cell epitopes of the target antigen; and at least one dose of (b) a second composition comprising (i) a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition; and (ii) a source of one or more CD8+ T cell epitopes of the target antigen, including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the first composition wherein the source of CD4+ and CD8+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; wherein the doses of the first and second compositions may be administered in either order.

3. A method according to claim 1 or 2, wherein the target antigen is derivable from an infectious pathogen.

4. A method according to claim 1 or 2, wherein the target antigen is a tumour antigen or autoantigen.

5. A method according to any preceding claim, wherein the recombinant poxvirus vector is of the modified vaccinia virus Ankara strain or derivative thereof.

6. A method according to any of claims 1 to 4, wherein the recombinant poxvirus vector is a **fowlpox** vector or derivative thereof.

7. A method according to any preceding claim, where the epitopes in or encoded by the first or second composition are provided in a sequence which does not occur naturally as the expressed product of a gene in the parental organism from which the target antigen may be derived.

8. A method according to any preceding claim, wherein the induced CD4 T cell response is of a $T_{H1\text{-}type}$.

9. A method according to any preceding claim, wherein the induced CD4 T cell response is of a gamma-**interferon**-secreting type.

10. A method according to any preceding claim, in which at least one dose of a composition is administered by an intradermal route.

11. A method according to any preceding claim, which comprises administering at least one dose of the first composition, followed by at least one dose of the second composition.

plurality of sequential doses of the first composition, followed by at least one dose of the second composition.

13. A method according to claim 12, which comprises administering three sequential doses of the first composition, followed by one dose of the second composition

14. A method according to any preceding claim for use in the prevention one of the following diseases: tuberculosis, HIV, malaria. H. pylori, influenza, hepatitis, CMV, viral infection, herpes virus-induced disease, leprosy, a disease caused by a non-malarial protozoan parasite such as toxoplasma, and cancer.

15. A method according to any of claims 1 to 13 for use in the treatment one of the following diseases: tuberculosis, persistent viral infection such as HIV and chronic hepatitis B and C, and cancer.

16. A method according to any preceding claim, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

17. A product which comprises: (a) a first composition comprising a source of one or more CD4+ T cell epitopes of a target antigen; and (b) a second composition comprising a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition, wherein the source of CD4+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector as a combined preparation for simultaneous, separate or sequential use for inducing a CD4+ T-cell response against a target antigen.

18. A product which comprises: (a) a first composition comprising a source of one or more CD4+ T cell epitopes and a source of one or more CD8+ T cell epitopes of a target antigen; and (b) a second composition comprising (i) a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition; and (ii) a source of one or more CD8+ T cell epitopes of the target antigen, including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the first composition wherein the source of CD4+ and CD8+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; as a combined preparation for simultaneous, separate or sequential use for inducing a combined CD4+ /CD8+ T cell immune response against the target antigen.

19. A product according to claim 17 or 18, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

20. The use of a product according to claim 17, 18 or 19, in the manufacture of a medicament for inducing a CD4+ T-cell response against a target antigen.

21. A medicament for boosting a primed CD4+ T cell response against at least one target antigen, comprising a source of one or more CD4+ T cell epitopes of the target antigen, wherein the source of CD4+ T cell epitopes is a non-replicating or a replication-impaired recombinant poxvirus vector.

22. A method of boosting a primed CD4+ T cell response, which method comprises administering a medicament according to claim 21.

23. The use of a recombinant non-replicating or replication-impaired pox virus vector in the manufacture of a medicament for boosting a CD4+ T cell immune response.

L5 ANSWER 9 OF 15 USPATFULL on STN
2003:200470 Vaccination method.
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Oxxon Pharmaccines, Ltd., Littlemore, UNITED KINGDOM (non-U.S. corporation)
US 2003138454 A1 20030724
APPLICATION: US 2002-79167 A1 20020219 (10)
PRIORITY: GB 1997-11957 19970609
GB 2000-23203 20000921
DOCUMENT TYPE: Utility; APPLICATION.

AB New methods and reagents for vaccination are described which generate a CD8 T cell immune response against malarial and other antigens such as viral and tumour antigens. Novel vaccination regimes are described which employ a priming composition and a boosting composition, the boosting composition comprising a non-replicating or replication-impaired pox virus vector carrying at least one CD8 T cell epitope which is also present in the priming composition. There is also provided a method of inducing a CD4+ T-cell response against a target antigen, by administering a composition comprising a source of one or more CD4+ T cell epitopes of the target antigen wherein the source of CD4+ epitopes is a non-replicating or replication impaired recombinant poxvirus vector. A method of inducing a combined CD4+ and CD8+ T cell response against a target antigen is also described herein.

CLM What is claimed is:

1. A method of inducing a CD4+ T-cell response against a target antigen in a mammal, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes of the target antigen; and at least one dose of (b) a second composition comprising a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition, wherein the source of CD4+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector, and wherein the doses of the first and second compositions may be administered in either order.

2. A method according to claim 1, wherein the target antigen is derivable from an infectious pathogen.

3. A method according to claim 1, wherein the target antigen is a tumour antigen or autoantigen.

4. A method according to claim 1, wherein the recombinant poxvirus vector is a modified vaccinia virus Ankara strain or derivative thereof.

5. A method according to claim 1, wherein the recombinant poxvirus vector is a **fowlpox** vector or derivative thereof.

6. A method according to claim 1, where the epitopes in or encoded by the first or second composition are provided in a sequence which does not occur naturally as the expressed product of a gene in the parental organism from which the target antigen may be derived.

7. A method according to claim 1, wherein the induced CD4 T cell response is of a $T_{H1\text{-}type}$.

8. A method according to claim 1, wherein the induced CD4 T cell response is of a gamma-**interferon**-secreting type.

9. A method according to any claim 1, in which at least one dose of a composition is administered by an intradermal route.

10. A method according to claim 1, which comprises administering at least one dose of the first composition, followed by at least one dose of the second composition.

11. A method according to claim 10, which comprises administering a plurality of sequential doses of the first composition, followed by at least one dose of the second composition.

12. A method according to claim 11, which comprises administering three sequential doses of the first composition, followed by one dose of the second composition.

13. A method according to claim 1, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

14. A method according to claim 1 wherein the target antigen is derived from a disease selected from the group consisting of: tuberculosis, HIV, malaria. H. pylori, influenza, hepatitis, CMV, viral infection, herpes virus-induced disease, leprosy, a disease caused by a non-malarial protozoan parasite such as toxoplasma, and cancer.

15. A method inducing a combined CD4+ and CD8+ T-cell response against a target antigen in a mammal, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes and a source of one or more CD8+ T cell epitopes of the target antigen; and at least one dose of (b) a second composition comprising (i) a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition; and (ii)

including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the first composition wherein the source of CD4+ and CD8+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; and wherein the doses of the first and second compositions may be administered in either order.

16. A method according to claim 15, wherein the target antigen is derivable from an infectious pathogen.

17. A method according to claim 15, wherein the target antigen is a tumour antigen or autoantigen.

18. A method according to claim 15, wherein the recombinant poxvirus vector is a modified vaccinia virus Ankara strain or derivative thereof.

19. A method according to claim 15, wherein the recombinant poxvirus vector is a **fowlpox** vector or derivative thereof.

20. A method according to claim 15, where the epitopes in or encoded by the first or second composition are provided in a sequence which does not occur naturally as the expressed product of a gene in the parental organism from which the target antigen may be derived.

21. A method according to claim 15, wherein the induced CD4 T cell response is of a $T_{H1\text{-}type}$.

22. A method according to claim 15, wherein the induced CD4 T cell response is of a gamma-**interferon**-secreting type.

23. A method according to any claim 15, in which at least one dose of a composition is administered by an intradermal route.

24. A method according to claim 15, which comprises administering at least one dose of the first composition, followed by at least one dose of the second composition.

25. A method according to claim 24, which comprises administering a plurality of sequential doses of the first composition, followed by at least one dose of the second composition.

26. A method according to claim 25, which comprises administering three sequential doses of the first composition, followed by one dose of the second composition.

27. A method according to claim 15, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

28. A method according to claim 15 wherein the target antigen is derived from a disease selected from the group consisting of: tuberculosis, HIV, malaria. H. pylori, influenza, hepatitis, CMV, viral infection, herpes virus-induced disease, leprosy, a disease caused by a non-malarial protozoan parasite such as toxoplasma, and cancer.

29. A method of inducing a CD4+ T-cell response against tuberculosis in a mammal, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes of tuberculosis; and at least one dose of (b) a second composition comprising a source of one or more CD4+ T cell epitopes of tuberculosis, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition, wherein the source of CD4+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector, and wherein the doses of the first and second compositions may be administered in either order.

30. A method according to claim 29, wherein the recombinant poxvirus vector is a modified vaccinia virus Ankara strain or derivative thereof.

31. A method according to claim 29, wherein the recombinant poxvirus vector is a **fowlpox** vector or derivative thereof.

32. A method according to any claim 29, in which at least one dose of a composition is administered by an intradermal route.

33. A method according to claim 29, which comprises administering at least one dose of the first composition, followed by at least one dose of the second composition.

34. A method according to claim 33, which comprises administering a plurality of sequential doses of the first composition, followed by at

35. A method according to claim 34, which comprises administering three sequential doses of the first composition, followed by one dose of the second composition.

36. A method according to claim 29, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

37. A method inducing a combined CD4+ and CD8+ T-cell response against tuberculosis in a mammal, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes and a source of one or more CD8+ T cell epitopes of tuberculosis; and at least one dose of (b) a second composition comprising (i) a source of one or more CD4+ T cell epitopes of tuberculosis, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition; and (ii) a source of one or more CD8+ T cell epitopes of the target antigen, including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the first composition wherein the source of CD4+ and CD8+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; and wherein the doses of the first and second compositions may be administered in either order.

38. A method according to claim 37, wherein the recombinant poxvirus vector is a modified vaccinia virus Ankara strain or derivative thereof.

39. A method according to claim 37, wherein the recombinant poxvirus vector is a **fowlpox** vector or derivative thereof.

40. A method according to any claim 37, in which at least one dose of a composition is administered by an intradermal route.

41. A method according to claim 37, which comprises administering at least one dose of the first composition, followed by at least one dose of the second composition.

42. A method according to claim 41, which comprises administering a plurality of sequential doses of the first composition, followed by at least one dose of the second composition.

43. A method according to claim 42, which comprises administering three sequential doses of the first composition, followed by one dose of the second composition.

44. A method according to claim 37, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

45. A method of inducing a CD4+ T-cell response against malaria in a mammal, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes of malaria; and at least one dose of (b) a second composition comprising a source of one or more CD4+ T cell epitopes of malaria, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition, wherein the source of CD4+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector, and wherein the doses of the first and second compositions may be administered in either order.

46. A method according to claim 45, wherein the recombinant poxvirus vector is a modified vaccinia virus Ankara strain or derivative thereof.

47. A method according to claim 45, wherein the recombinant poxvirus vector is a **fowlpox** vector or derivative thereof.

48. A method according to any claim 45, in which at least one dose of a composition is administered by an intradermal route.

49. A method according to claim 45, which comprises administering at least one dose of the first composition, followed by at least one dose of the second composition.

50. A method according to claim 45, which comprises administering a plurality of sequential doses of the first composition, followed by at least one dose of the second composition.

51. A method according to claim 45, which comprises administering three sequential doses of the first composition, followed by one dose of the second composition.

52. A method according to claim 51, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

53. A method inducing a combined CD4+ and CD8+ T-cell response against malaria in a mammal, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes and a source of one or more CD8+ T cell epitopes of malaria; and at least one dose of (b) a second composition comprising (i) a source of one or more CD4+ T cell epitopes of malaria, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition; and (ii) a source of one or more CD8+ T cell epitopes of malaria, including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the first composition wherein the source of CD4+ and CD8+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; and wherein the doses of the first and second compositions may be administered in either order.

54. A method according to claim 53, wherein the recombinant poxvirus vector is a modified vaccinia virus Ankara strain or derivative thereof.

55. A method according to claim 53, wherein the recombinant poxvirus vector is a **fowlpox** vector or derivative thereof.

56. A method according to any claim 53, in which at least one dose of a composition is administered by an intradermal route.

57. A method according to claim 53, which comprises administering at least one dose of the first composition, followed by at least one dose of the second composition.

58. A method according to claim 57, which comprises administering a plurality of sequential doses of the first composition, followed by at least one dose of the second composition.

59. A method according to claim 58, which comprises administering three sequential doses of the first composition, followed by one dose of the second composition.

60. A method according to claim 53, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

61. A method of inducing a CD4+ T-cell response against malaria in a human, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes of malaria; and at least one dose of (b) a second composition comprising a source of one or more CD4+ T cell epitopes of malaria, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition, wherein the source of CD4+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector, and wherein the doses of the first and second compositions may be administered in either order.

62. A method inducing a combined CD4+ and CD8+ T-cell response against malaria in a human, which comprises the step of administering at least one dose of: (a) a first composition comprising a source of one or more CD4+ T cell epitopes and a source of one or more CD8+ T cell epitopes of malaria; and at least one dose of (b) a second composition comprising (i) a source of one or more CD4+ T cell epitopes of malaria, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition; and (ii) a source of one or more CD8+ T cell epitopes of the target antigen, including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the first composition wherein the source of CD4+ and CD8+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; and wherein the doses of the first and second compositions may be administered in either order.

63. A method of boosting a primed CD4+ T cell response against at least one target antigen in a mammal, which comprises administering a source of one or more CD4+ T cell epitopes of the target antigen, wherein the source of CD4+ T cell epitopes is a non-replicating or a replication-impaired recombinant poxvirus vector.

64. A method of boosting a primed CD4+ and CD8+ T cell response against at least one target antigen in a mammal, which comprises administering a source of one or more CD4+ and CD8+ T cell epitopes of the target antigen, wherein the source of CD4+ and CD8+ T cell epitopes is anon-replicating or a replication-impaired recombinant poxvirus vector.

65. A product which comprises: (a) a first composition comprising a source of one or more CD4+ T cell epitopes of a target antigen; and (b) a second composition comprising a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition, wherein the source of CD4+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; and the first composition and the second composition are a combined preparation for simultaneous, separate or sequential use for inducing a CD4+ T-cell response against a target antigen.

66. A product according to claim 65, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

67. A product which comprises: (a) a first composition comprising a source of one or more CD4+ T cell epitopes and a source of one or more CD8+ T cell epitopes of a target antigen; and (b) a second composition comprising (i) a source of one or more CD4+ T cell epitopes of the target antigen, including at least one CD4+ T cell epitope which is the same as a CD4+ T cell epitope of the first composition; and (ii) a source of one or more CD8+ T cell epitopes of the target antigen, including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the first composition wherein the source of CD4+ and CD8+ epitopes for the first and/or second composition is a non-replicating or replication impaired recombinant poxvirus vector; and the first composition and the second composition are a combined preparation for simultaneous, separate or sequential use for inducing a combined CD4+/CD8+ T cell immune response against the target antigen.

68. A product according to claim 67, with the proviso that if the source of epitopes in (a) is a viral vector, the viral vector in (b) is derived from a different virus.

L5 ANSWER 10 OF 15 USPATFULL on STN
2003:29866 Cd40 ligand adjuvant for respiratory syncytial virus.
Tripp, Ralph A, Decatur, GA, UNITED STATES
Anderson, Larry J, Atlanta, GA, UNITED STATES
Brown, Michael P, St Georges, South Autralia, AUSTRALIA
US 2003021808 A1 20030130
APPLICATION: US 2002-182093 A1 20020725 (10)
WO 2001-US3584 20010202
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides methods and adjuvants for enhancing an immune response to RSV in a host, wherein the methods and adjuvants comprise a source of a CD40 binding protein. Preferably, the CD40 binding protein is CD40L and the source is a vector comprising a promoter operatively linked to a CD40L coding region. The enhanced immune response produced by the adjuvants and methods of the current invention includes both increased expression of Th1 cytokines and increased production of antibody.
CLM What is claimed is:
1. A method for enhancing an immune response to respiratory syncytial virus (RSV), said method comprising administering to a host an effective amount of an RSV vaccine and an effective amount of a source of a CD40 binding protein.

2. The method of claim 1, wherein the CD40 binding protein is selected from the group consisting of CD40 ligand, a CD40 ligand homologue, monoclonal antibodies that specifically bind CD40, and combinations thereof.

3. The method of claim 2, wherein the CD40 binding protein is CD40 ligand.

4. The method of claim 3, wherein the source is a vector comprising a promoter operatively linked to nucleic acids encoding the CD40 ligand.

5. The method of claim 4, wherein the vector is a plasmid.

6. The method of claim 4, wherein the vector is an adenovirus vector.

7. The method of claim 4, wherein the host is a human.

8. The method of claim 4, wherein the host is a human whose genome comprises a wild type CD40 ligand gene.

9. The method of claim 4, wherein the RSV vaccine is selected from a vaccine comprising an RSV F gene product or a vaccine comprising a

10. The method of claim 4, wherein the RSV vaccine comprises an RSV G gene product or a vaccine comprising a vector comprising a nucleic acid sequence encoding the RSV G gene.

11. The method of claim 1, wherein the immune response comprises a Th1 **cytokine** immune response.

12. The method of claim 1, wherein the immune response comprises an antibody response.

13. An adjuvant for enhancing an immune response of a host to a respiratory syncytial virus (RSV) vaccine comprising an effective amount of a source of a CD40 binding protein.

14. The adjuvant of claim 13, wherein the CD40 binding protein is selected from the group consisting of CD40 ligand, a CD40 ligand homologue, monoclonal antibodies that specifically bind CD40, and combinations thereof.

15. The adjuvant of claim 14, wherein the CD40 binding protein is CD40 ligand.

16. The adjuvant of claim 15, wherein the source is a vector comprising a promoter operatively linked to nucleic acids encoding the CD40 ligand.

17. The adjuvant of claim 16, wherein the vector is a plasmid.

18. The adjuvant of claim 16, wherein the vector is an adenovirus vector.

19. The adjuvant of claim 15, wherein the host is a human.

20. An adjuvant for enhancing a Th1 immune response to an RSV antigen of a human whose genome comprises a wild type CD40 ligand gene, said adjuvant comprising an effective amount of an adenovirus vector comprising a cytomegalovirus promoter operatively linked to nucleic acids encoding CD40 ligand.

21. A method for immunizing a host against disease caused by infection with respiratory syncytial virus (RSV), said method comprising administering to said host an effective amount of an RSV vaccine and an effective amount of a vector comprising a promoter operatively linked to nucleotide sequences encoding CD40 ligand.

22. The method of claim 21, wherein said host is a human.

23. The method of claim 21, wherein the RSV vaccine comprises an RSV F gene product or a vector comprising a nucleic acid sequence encoding the RSV F gene product.

24. The method of claim 21, wherein the RSV vaccine is selected from a vaccine comprising an RSV G gene product or a vaccine comprising a vector comprising a nucleic acid sequence encoding the RSV G gene.

25. The method of claim 21, wherein the vector is a plasmid.

26. The method of claim 21, wherein the vector is an adenovirus vector.

27. The method of claim 21, wherein the vector is an avipox vector.

28. The method of claim 27, wherein the vector is a canarypox vector.

29. The method of claim 27, wherein the vector is a **fowlpox** vector.

L5 ANSWER 11 OF 15 USPATFULL on STN
2002:340150 Recombinant swinepox virus.
Cochran, Mark D., Carlsbad, CA, United States
Junker, David E., San Diego, CA, United States
Syntro Corporation, San Diego, CA, United States (U.S. corporation)
US 6497882 B1 20021224
APPLICATION: US 1995-472679 19950607 (8)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a recombinant swinepox virus comprising a foreign DNA sequence inserted into the swinepox virus genomic DNA, wherein the foreign DNA sequence is inserted within a HindIII K fragment of the swinepox virus genomic DNA and is capable of being expressed in a swinepox virus infected host cell.

The invention further provides homology vectors, vaccines and methods of

CLM What is claimed is:

1. A recombinant swinepox virus comprising a foreign DNA inserted into a swinepox virus genome, wherein the foreign DNA is inserted within a region corresponding to a 3.2 kB subfragment which contains a HindIII site and an EcoRI site within the HindIII K fragment of the swinepox virus genome and is capable of being expressed in a host cell into which the virus is introduced.

2. The recombinant swinepox virus of claim 1, wherein the foreign DNA is inserted into an open reading frame within the region corresponding to the 3.2 kB subfragment.

3. The recombinant swinepox virus of claim 2, wherein the foreign DNA is inserted into a B18R gene.

4. The recombinant swinepox virus of claim 2, wherein the foreign DNA is inserted into a B4R gene.

5. The recombinant swinepox virus of claim 1, wherein the foreign DNA encodes a polypeptide.

6. The recombinant swinepox virus of claim 5, wherein the polypeptide is antigenic.

7. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from a virus which is selected from the group consisting of: human herpesvirus, herpes simplex virus-1, herpes simplex virus-2, human cytomegalovirus, Epstein-Barr virus, varicella-zoster virus, human herpesvirus-6, human herpesvirus-7, human influenza, human immunodeficiency virus, rabies virus, measles virus, hepatitis B virus, and hepatitis C virus.

8. The recombinant swinepox virus of claim 5, wherein the polypeptide is hepatitis B virus core protein or hepatitis B virus surface protein.

9. The recombinant swinepox virus of claim 5, wherein the polypeptide is equine influenza virus neuraminidase or equine influenza virus hemagglutinin.

10. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: equine influenza virus type A/Alaska 91 neuraminidase, equine influenza virus type A/Kentucky 92 neuraminidase, equine influenza virus type A/Prague 56 neuraminidase, equine influenza virus type A/Miami 63 neuraminidase, equine influenza virus type A/Kentucky 81 neuraminidase, equine herpesvirus type 1 glycoprotein B, and equine herpesvirus type 1 glycoprotein D.

11. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: hog cholera virus glycoprotein E1, hog cholera virus glycoprotein E2, swine influenza virus hemagglutinin, swine influenza virus neuraminidase, swine influenza virus matrix, swine influenza virus nucleoprotein, pseudorabies virus glycoprotein B, pseudorabies virus glycoprotein C, pseudorabies virus glycoprotein D, and PRRS virus ORF7.

12. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: Infectious bovine rhinotracheitis virus gE, bovine respiratory syncytial virus attachment protein (BRSV G), bovine respiratory syncytial virus fusion protein (BRSV F), bovine respiratory syncytial virus nucleocapsid protein (BRSV N), bovine parainfluenza virus type 3 fusion protein, and the bovine parainfluenza virus type 3 hemagglutinin neuraminidase.

13. The recombinant swinepox virus of claim 5, wherein the polypeptide is bovine viral diarrhea virus (BVDV) glycoprotein 48 or bovine viral diarrhea virus glycoprotein 53.

14. The recombinant swinepox virus of claim 5, wherein the polypeptide is selected from the group consisting of: feline immunodeficiency virus gag, feline immunodeficiency virus env, infectious laryngotracheitis virus glycoprotein B, infectious laryngotracheitis virus glycoprotein I, infectious laryngotracheitis virus glycoprotein D, infectious bovine rhinotracheitis virus glycoprotein G, infectious bovine rhinotracheitis virus glycoprotein E, pseudorabies virus glycoprotein 50, pseudorabies virus II glycoprotein B, pseudorabies virus III glycoprotein C, pseudorabies virus glycoprotein E, pseudorabies virus glycoprotein H, Marek's disease virus glycoprotein A, Marek's disease virus glycoprotein B, Marek's disease virus glycoprotein D, Newcastle disease virus hemagglutinin, Newcastle disease virus neuraminidase, Newcastle disease virus fusion, infectious bursal disease virus VP2, infectious bursal disease virus VP3, infectious bursal disease virus VP4, infectious bursal disease virus polyprotein, infectious bronchitis virus spike, and

15. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from an organism selected from the group consisting of Streptococcus equi, equine infectious anemia virus, equine encephalitis virus, equine rhinovirus and equine rotavirus.

16. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from an organism selected from the group consisting of avian encephalomyelitis virus, avian reovirus, avian paramyxovirus, avian influenza virus, avian adenovirus, **fowlpox** virus, avian coronavirus, avian rotavirus, chick anemia virus, Salmonella spp., E. coli, Pasteurella spp., Bordetella spp., Eimeria spp., Histomonas spp., Trichomonas spp., poultry. nematodes, cestodes, trematodes, poultry mites, poultry lice and poultry protozoa.

17. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from an organism selected from the group consisting of canine herpesvirus, canine distemper virus, canine adenovirus type 1, canine adenovirus type 2, parainfluenza virus, Leptospira canicola, parvovirus, coronavirus, Borrelia burgdorferi, canine herpesvirus, Bordetella bronchiseptica, Dirofilaria immitis and rabies virus.

18. The recombinant swinepox virus of claim 5, wherein the polypeptide is derived from a virus selected from the group consisting of feline leukemia virus, feline immunodeficiency virus, feline herpesvirus and feline infectious peritonitis virus.

19. The recombinant swinepox virus of claim 1, further comprising a foreign DNA which encodes a detectable marker.

20. The recombinant swinepox virus of claim 19, wherein the detectable marker is E. coli beta-galactosidase.

21. The recombinant swinepox virus of claim 19, wherein the detectable marker is E. coli beta-glucuronidase.

22. The recombinant swinepox virus of claim 1, wherein the foreign DNA encodes a **cytokine**.

23. The recombinant swinepox virus of claim 22, wherein the **cytokine** is chicken myelomonocytic growth factor (cMGF) or chicken **interferon** (cIFN).

24. The recombinant swinepox virus of claim 22, wherein the **cytokine** is selected from the group consisting of interleukin-2, interleukin-6, interleukin-12, interferons, and granulocyte-macrophage colony stimulating factor.

25. The recombinant swinepox virus of claim 1, wherein the foreign DNA is under the control of an endogenous poxvirus promoter.

26. The recombinant swinepox virus of claim 1, wherein the foreign DNA is under the control of a heterologous promoter.

27. The recombinant swinepox virus of claim 1, wherein the promoter is: pox synthetic late promoter 1, pox synthetic late promoter 2 early promoter 2, pox O1L promoter, pox I4L promoter, pox I3L promoter, pox I2L promoter, pox I1L promoter, or pox E10R promoter.

28. A vaccine which comprises an effective immunizing amount of the recombinant swinepox virus of claim 1, and a suitable carrier.

29. A method of immunizing an animal against an animal pathogen which comprises administering to the animal an effective immunizing dose of the vaccine of claim 28.

30. A homology vector for producing a recombinant swinepox virus by inserting foreign DNA into a swinepox virus genome which comprises a double-stranded DNA consisting essentially of: a) double stranded foreign DNA not usually present within the swinepox virus genome; b) at one end the foreign DNA, double-stranded swinepox virus DNA homologous to the virus genome located at one side of the HindIII K fragment of the coding region of the swinepox virus genome; and c) at the other end of the foreign DNA, double-stranded swinepox virus DNA homologous to the virus genome located at the other side of the HindIII K fragment of the coding region of the swinepox virus genome.

31. The homology vector of claim 30, wherein the foreign DNA encodes a **cytokine**.

32. The homology vector of claim 31, wherein the **cytokine** is chicken myelomonocytic growth factor (cMGF) or chicken **interferon** (cIFN).

33. The homology vector of claim 30, wherein the foreign DNA encodes a polypeptide.

34. A homology vector of claim 33, wherein the polypeptide is antigenic.

35. The homology vector of claim 30, wherein the foreign DNA is under control of a promoter.

L5 ANSWER 12 OF 15 USPATFULL on STN
2002:152217 Recombinant infectious bovine rhinotracheitis virus.
Cochran, Mark D., Carlsbad, CA, United States
Syntro Corporation, San Diego, CA, United States (U.S. corporation)
US 6410033 B1 20020625
WO 9521261 19950810
APPLICATION: US 1996-379647 19960805 (8)
WO 1995-US1491 19950202 19960805 PCT 371 date
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a recombinant infectious bovine rhinotracheitis designated S-IBR-052 (ATCC Accession No. VR 2443). The present invention also provides a vaccine which comprises an effective immunizing amount of the recombinant infectious bovine rhinotracheitis virus designated S-IBR-052 and a suitable carrier.

The present invention provides homology vectors, methods of immunization and a method of distinguishing an animal vaccinated with the vaccines of the present invention from an animal infected with a naturally-occurring infectious bovine rhinotracheitis virus.
CLM What is claimed is:
1. A recombinant infectious bovine rhinotracheitis virus comprising a foreign DNA sequence inserted into an infectious bovine rhinotracheitis viral genome, wherein the foreign DNA sequence is inserted within the BamHI C fragment of the infectious bovine rhinotracheitis viral genome and is capable of being expressed in an infectious bovine rhinotracheitis virus infected host cell.

2. The recombinant infectious bovine rhinotracheitis virus of claim 1, wherein the foreign DNA sequence is inserted within the largest BamHI-KpnI subfragment of the BamHI C fragment of the infectious bovine rhinotracheitis viral genome.

3. The recombinant infectious bovine rhinotracheitis virus of claim 2, wherein the foreign DNA sequence is inserted within a HindIII site located within the largest BamHI-KpnI subfragment of the infectious bovine rhinotracheitis viral genome.

4. The recombinant infectious bovine rhinotracheitis virus of claim 2, wherein the foreign DNA sequence is inserted within an XbaI site located within the largest BamHI-KpnI subfragment of the infectious bovine rhinotracheitis viral genome.

5. The recombinant infectious bovine rhinotracheitis virus of claim 1, wherein the foreign DNA sequence is inserted within the smallest KpnI-BamHI subfragment of the BamHI C fragment of the infectious bovine rhinotracheitis viral genome.

6. The recombinant infectious bovine rhinotracheitis virus of claim 5, wherein the foreign DNA sequence is inserted within an EcoRV site located within the smallest KpnI-BamHI subfragment of the infectious bovine rhinotracheitis viral genome.

7. The recombinant infectious bovine rhinotracheitis virus of claim 1, further comprising a deletion in a non-essential region of the infectious bovine rhinotracheitis viral genome.

8. The recombinant infectious bovine rhinotracheitis virus of claim 7, wherein the deletion is in a US2 gene, a gG gene or a gE gene region.

9. The recombinant infectious bovine rhinotracheitis virus of claim 1, wherein the foreign DNA sequence encodes a polypeptide.

10. The recombinant infectious bovine rhinotracheitis virus of claim 9, wherein the polypeptide is antigenic in an animal into which the recombinant infectious bovine rhinotracheitis virus is introduced.

11. The recombinant infectious bovine rhinotracheitis virus of claim 9, wherein the polypeptide is E. coli beta-galactosidase.

12. The recombinant infectious bovine rhinotracheitis virus of claim 1, wherein the foreign DNA sequence encodes a **cytokine** or **cytokine** receptor.

13. The recombinant infectious bovine rhinotracheitis virus of claim 12, wherein the **cytokine** or **cytokine** receptor is selected from the group consisting of: chicken myelomonocytic growth factor (cMGF), chicken **interferon** (cIFN), interleukin-2, interleukin-6, interleukin-12, interferons, granulocyte-macrophage colony stimulating factors, transforming growth factor beta, epidermal growth factors, fibroblast growth factors, hepatocyte growth factor, insulin-like growth factors, B-nerve growth factor, platelet-derived growth factor, vascular endothelial growth factor, interleukin 1, IL-1 receptor antagonist, interleukin 3, interleukin 4, interleukin 5, IL-6 soluble receptor, interleukin 7, interleukin 8, interleukin 9, interleukin 10, interleukin 11, interleukin 13, angiogenin, chemokines, colony stimulating factors, erythropoietin, **interferon** gamma, leukemia inhibitory factor, oncostatin M, pleiotrophin, secretory leukocyte protease inhibitor, stem cell factor, tumor necrosis factors, soluble TNF receptors and interleukin receptors.

14. The recombinant infectious bovine rhinotracheitis virus of claim 10, wherein the antigenic polypeptide is an equine influenza virus neuroaminidase or an equine influenza virus hemagglutinin.

15. The recombinant infectious bovine rhinotracheiti virus of claim 10, wherein the antigenic polypeptide is selected from the group consisting of equine influenza virus type A/Alaska 91 neuraminidase, equine influenza virus type A/Alaska 91 hemagglutinin, equine influenza virus type A/Prague 56 neuraminidase, equine influenza virus type A/Prague 56 hemagglutinin, equine influenza virus type A/Miami 63 neuraminidase, equine influenza virus type A/Miami 63 hemagglutinin, equine influenza virus type A/Kentucky 81 neuraminidase equine influenza virus type A/Kentucky 81 hemagglutinin, equine herpesvirus type 1 glycoprotein B, and equine herpesvirus type 1 glycoprotein D.

16. The recombinant infectious bovine rhinotracheitis virus of claim 10, wherein the antigenic polypeptide is selected from the group consisting of hog cholera virus gE1, hog cholera virus gE2, swine influenza virus hemagglutinin, neuraminidase, matrix protein, nucleoprotein, pseudorabies virus gB, pseudorabies virus gC, pseudorabies virus gD, and PRRS virus ORF7.

17. The recombinant infectious bovine rhinotracheitis virus of claim 10, wherein the antigenic polypeptide is selected from the group consisting of: bovine respiratory syncytial virus attachment protein (BRSV G), bovine respiratory syncytial virus fusion protein (BRSV F), bovine respiratory syncytial virus nucleocapsid protein (BRSV N), bovine coronavirus, bovine rotavirus glycoprotein 38, bovine parainfluenza virus type 3 fusion protein, and bovine parainfluenza virus type 3 hemagglutinin neuraminidase.

18. The recombinant infectious bovine rhinotracheitis virus of claim 10, wherein the antigenic polypeptide is bovine viral diarrhea virus (BVDV) glycoprotein 48 or bovine viral diarrhea virus (BVDV) glycoprotein 53.

19. The recombinant infectious bovine rhinotracheitis virus of claim 10, wherein the antigenic polypeptide is selected from the group consisting of Marek's disease virus gA, Marek's disease virus gB, Marek's disease virus gD, Newcastle disease virus HN, Newcastle disease virus F, infectious laryngotracheitis virus gB, infectious laryngotracheitis virus gI, infectious laryngotracheitis virus gD, infectious bursal disease virus VP2, infectious bursal disease virus VP3, infectious bursal disease virus VP4, infectious bursal disease virus polyprotein, infectious bronchitis virus spike, infectious bronchitis virus matrix and chick anemia virus matrix.

20. The recombinant infectious bovine rhinotracheitis virus of claim 1, wherein the foreign DNA sequence is under the control of an endogenous infectious bovine rhinotracheitis virus promoter.

21. The recombinant infectious bovine rhinotracheitis virus of claim 20, wherein the foreign DNA sequence is under the control of a heterologous herpesvirus promoter.

22. The recombinant infectious bovine rhinotracheitis virus of claim 21, wherein the promoter is selected from the group consisting of a herpes simplex virus type 1 (HSV-1) ICP4 protein promoter, an HSV-1 TK promoter, a pseudorabies virus (PRV) glycoprotein X promoter, a PRV gX promoter, an HCMV immediate early promoter, a Marek's disease virus gA promoter, a Marek's disease virus gB promoter, a Marek's disease virus gD promoter, an infectious laryngotracheitis virus gB promoter, a BHV-1.1 VP8 promoter and an infectious laryngotracheitis virus gD promoter.

23. A vaccine which comprises an effective immunizing amount of the

carrier.

24. The vaccine of claim 23, wherein the carrier is a physiologically balanced culture medium containing stabilizing agents.

25. The vaccine of claim 23, wherein the effective immunizing amount is from about 10^3 to about 10^8 PFU/dose.

26. The vaccine of claim 25, wherein the effective immunizing amount is from about 10^4 to about 10^7 PFU/dose.

27. The vaccine of claim 25, wherein the effective immunizing amount is from about 10^4 to about 10^6 PFU/dose.

28. A method of immunizing an animal against disease caused by infectious bovine rhinotracheitis virus which comprises administering to the animal an effective immunizing dose of the vaccine of claim 23.

29. The recombinant infectious bovine rhinotracheitis virus of claim 10, wherein the antigenic polypeptide is from an organism or virus selected from the group consisting of Streptococcus equi, equine infectious anemia virus, equine encephalitis virus, equine rhinovirus and equine rotavirus.

30. The recombinant infectious bovine rhinotracheitis virus of claim 10, wherein the antigenic polypeptide is from an organism or virus selected from the group consisting of avian encephalomyelitis virus, avian reovirus, avian paramyxovirus, avian influenza virus, avian adenovirus, **fowlpox** virus, avian coronavirus, avian rotavirus, chick anemia virus, Salmonella spp., E. coli, Pasteurella spp., Bordetella spp., Eimeria spp., Histomonas spp., Trichomonas spp., poultry nematodes, cestodes, trematodes, poultry mites, poultry lice and poultry protozoa.

L5 ANSWER 13 OF 15 USPATFULL on STN
2000:141886 Recombinant fowlpox viruses and uses thereof.
Cochran, Mark D., 4506 Horizon Dr., Carlsbad, CA, United States 92008
Junker, David E., 6901 Galewood St., San Diego, CA, United States 92120
US 6136318 20001024
APPLICATION: US 1995-486414 19950607 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a recombinant fowlpox virus comprising a foreign DNA sequence inserted into the fowlpox virus genomic DNA, wherein the foreign DNA sequence is inserted within a 3.5 kB EcoRI fragment of the fowlpox virus genomic DNA and is capable of being expressed in a fowlpox virus infected host cell. The invention further provides homology vectors, vaccines and methods of immunization.

CLM What is claimed is:
1. A recombinant **fowlpox** virus comprising a foreign DNA inserted into a **fowlpox** virus genome, wherein the foreign DNA is inserted within a region of the genome which corresponds to a 3.5 kb EcoRI fragment within a SalI C fragment and PstI F fragment of the **fowlpox** virus genome and is capable of being expressed in a host cell into which the virus is introduced.

2. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is inserted within a HpaI site within the region of the genome which corresponds to the 3.5 kb EcoRI fragment.

3. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA sequence encodes a polypeptide.

4. The recombinant **fowlpox** virus of claim 3, wherein the polypeptide is antigenic.

5. The recombinant **fowlpox** virus of claim 3, further comprising a foreign DNA sequence which encodes a detectable marker.

6. The recombinant **fowlpox** virus of claim 5, wherein the detectable marker is E. coli beta-galactosidase.

7. The recombinant **fowlpox** virus of claim 5, wherein the detectable marker is E. coli beta-glucuronidase.

8. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA sequence encodes a **cytokine**.

9. The recombinant **fowlpox** virus of claim 8, wherein the **cytokine** is chicken myelomonocytic growth factor (cMGF) or chicken **interferon** (cIFN).

sequence encodes an antigenic polypeptide which is selected from the group consisting of: infectious laryngotracheitis virus glycoprotein B, infectious laryngotracheitis virus glycoprotein D, Marek's disease virus glycoprotein D, Marek's disease virus glycoprotein B, Newcastle disease virus hemagglutinin, Newcastle disease virus neuraminidase, and Newcastle disease virus fusion protein.

11. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA sequence is under control of an endogenous upstream poxvirus promoter.

12. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA sequence is under control of a heterologous upstream promoter.

13. The recombinant **fowlpox** virus of claim 12, wherein the promoter is a synthetic pox viral promoter.

14. The recombinant **fowlpox** virus of claim 1, designated S-FPV-082.

15. A vaccine for immunizing an animal which comprises an effective immunizing amount of the recombinant **fowlpox** virus of claim 1 and a suitable carrier.

16. A method of immunizing an animal against an animal pathogen which comprises administering to the animal an effective immunizing dose of the vaccine of claim 15.

17. A method of enhancing an avian immune response which comprises administering to an avian an effective dose of the recombinant **fowlpox** virus of claim 1 and a suitable carrier.

18. The recombinant **fowlpox** virus of claim 3, wherein the synthetic pox viral promoter is selected from the group consisting of: pox synthetic late promoter 1, pox synthetic late promoter 2 early promoter 2, pox synthetic early promoter 1 late promoter 2, and pox synthetic early promoter 1.

19. A recombinant **fowlpox** virus designated S-FPV-085.

20. A recombinant **fowlpox** virus designated S-FPV-097, ATCC Accession No. VR 2446.

21. A recombinant **fowlpox** virus designated S-FPV-101.

22. A vaccine which comprises an effective immunizing amount of the recombinant **fowlpox** virus of any of claims 14, 19, 20, or 24 and a suitable carrier.

23. The vaccine of claim 22, wherein the carrier is a physiologically balanced culture medium containing stabilizing agents.

24. The vaccine of claim 22, wherein the effective immunizing amount is about 10^2 to about 10^9 PFU/dose.

25. The vaccine of claim 22, wherein the effective immunizing amount is about 10^3 to about 10^5 PFU/dose.

26. A method of immunizing an animal against **fowlpox** virus and Newcastle disease virus which comprises administering to the animal an effective immunizing dose of the vaccine of claim 22.

27. The method of claim 26, wherein the animal is an avian.

28. The method of claim 27, wherein the avian is a chicken.

29. The method of claim 26, wherein the vaccine is administered intramuscularly, intraperitoneally, intravenously, intradermal, intranasally, orally, ocularly, or inovo.

L5 ANSWER 14 OF 15 USPATFULL on STN
1999:163226 Recombinant fowlpox viruses and uses thereof.
Cochran, Mark D., Carlsbad, CA, United States
Junker, David E., San Diego, CA, United States
Syntro Corporation, Lenexa, KS, United States (U.S. corporation)
US 6001369 19991214
APPLICATION: US 1995-477459 19950607 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a recombinant fowlpox virus comprising a foreign DNA sequence inserted into the fowlpox virus genomic DNA, wherein the foreign DNA sequence is inserted within a 4.2 kB EcoRI fragment of the fowlpox virus genomic DNA and is capable of being expressed in a fowlpox

vectors, vaccines and methods of immunization.

CLM What is claimed is:

1. A recombinant **fowlpox** virus comprising a foreign DNA inserted into a **fowlpox** virus genome, wherein the foreign DNA is inserted within a site present in the **fowlpox** virus genome, which site is also present in a 4.2 kB EcoRI fragment of the **fowlpox** virus genome and wherein the foreign DNA is capable of being expressed in a host cell into which the virus is introduced.

2. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is inserted within a StuI site within the region which corresponds to the 4.2 kB EcoRI fragment.

3. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA encodes a polypeptide.

4. The recombinant **fowlpox** virus of claim 3, wherein the polypeptide is antigenic.

5. The recombinant **fowlpox** virus of claim 4, wherein the foreign DNA encodes an antigenic polypeptide which is selected from the group consisting of: infectious laryngotracheitis virus glycoprotein B, infectious laryngotracheitis virus glycoprotein D, marek's disease virus glycoprotein D, marek's disease virus glycoprotein B, newcastle disease virus hemagglutin in,newcastle disease virus neuraminadase, and newcastle disease virus fusion.

6. The recombinant **fowlpox** virus of claim 3, further comprising a foreign DNA sequence which encodes a detectable marker.

7. The recombinant **fowlpox** virus of claim 6, wherein the detectable marker is E. coli beta-galactosidase.

8. The recombinant **fowlpox** virus of claim 6, wherein the detectable marker is E. coli beta-glucuronidase.

9. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA encodes a **cytokine**.

10. The recombinant **fowlpox** virus of claim 9, wherein the **cytokine** is chicken myelomonocytic growth factor (cMGF) or chicken **interferon** (cIFN).

11. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is under control of an endogenous upstream poxvirus promoter.

12. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is under control of a heterologous upstream promoter.

13. The recombinant **fowlpox** virus of claim 12, wherein the promoter is a synthetic pox viral promoter.

14. The recombinant **fowlpox** virus of claim 13, wherein the synthetic pox viral promoter is: pox synthetic late promoter 1, pox synthetic late promoter 2 early promoter 2, pox synthetic early promoter 1 late promoter 2, or pox synthetic early promoter 1.

15. The recombinant **fowlpox** virus of claim 1, designated S-FPV-083.

16. A vaccine for immunizing an animal which comprises an effective immunizing amount of the recombinant **fowlpox** virus of claim 1 and a suitable carrier.

17. A method of immunizing an animal against an animal pathogen which comprises administering to the animal an effective immunizing dose of the vaccine of claim 16.

L5 ANSWER 15 OF 15 USPATFULL on STN

1999:81550 Recombinant fowlpox viruses and uses thereof.

Cochran, Mark D., Carlsbad, CA, United States
Junker, David E., San Diego, CA, United States
Syntro Corporation, Lenexa, KS, United States (U.S. corporation)

US 5925358 19990720

APPLICATION: US 1995-484575 19950607 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a recombinant fowlpox virus comprising a foreign DNA sequence inserted into the fowlpox virus genomic DNA, wherein the foreign DNA sequence is inserted within a 2.8 kB EcoRI fragment of the fowlpox virus genomic DNA and is capable of being expressed in a fowlpox virus infected host cell. The invention further provides homology

CLM What is claimed is:

1. A recombinant **fowlpox** virus comprising a foreign DNA inserted into a **fowlpox** virus genome, wherein the foreign DNA is inserted within a region corresponding to a 2.8 kB EcoRI fragment of the **fowlpox** virus genome and is capable of being expressed in a host cell into which the virus is introduced.

2. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is inserted within a SnaBI site within the region which corresponds to the 2.8 kB EcoRI fragment.

3. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA encodes a polypeptide.

4. The recombinant **fowlpox** virus of claim 3, wherein the polypeptide is antigenic.

5. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is hepatitis B virus core protein or hepatitis B virus surface protein.

6. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is equine influenza virus neuraminidase or hemagglutinin.

7. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is selected from the group consisting of: equine influenza virus type A/Alaska 91 neuraminidase, equine influenza virus type A/Kentucky 92 neuraminidase, equine influenza virus type A/Prague 56 neuraminidase, equine influenza virus type A/Miami 63 neuraminidase, equine influenza virus type A/Kentucky 81 neuraminidase, equine herpesvirus type 1 glycoprotein B, and equine herpesvirus type 1 glycoprotein D.

8. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is selected from the group consisting of: hog cholera virus glycoprotein E1, hog cholera virus glycoprotein E2, swine influenza virus hemagglutinin, neuraminidase, matrix and nucleoprotein, pseudorabies virus glycoprotein B, glycoprotein C and glycoprotein D, and PRRS virus ORF7.

9. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is selected from the group consisting of: Infectious bovine rhinotracheitis virus gE, bovine respiratory syncytial virus attachment protein (BRSV G), bovine respiratory syncytial virus fusion protein (BRSV F), bovine respiratory syncytial virus nucleocapsid protein (BRSV N), bovine parainfluenza virus type 3 fusion protein, and the bovine parainfluenza virus type 3 hemagglutinin neuraminidase.

10. The recombinant **fowlpox** virus of claim 4, wherein the antigenic polypeptide is bovine viral diarrhea virus (BVDV) glycoprotein 48 or glycoprotein 53.

11. The recombinant **fowlpox** virus of claim 4, wherein the foreign DNA sequence encodes an antigenic polypeptide which is selected from the group consisting of: feline immunodeficiency virus gag, feline immunodeficiency virus env, infectious laryngotracheitis virus glycoprotein B, infectious laryngotracheitis virus glycoprotein I, infectious laryngotracheitis virus glycoprotein D, infectious bovine rhinotracheitis virus glycoprotein G, infectious bovine rhinotracheitis virus glycoprotein E, pseudorabies virus glycoprotein 50, pseudorabies virus II glycoprotein B, pseudorabies virus III glycoprotein C, pseudorabies virus glycoprotein E, pseudorabies virus glycoprotein H, marek's disease virus glycoprotein A, marek's disease virus glycoprotein B, marek's disease virus glycoprotein D, newcastle disease virus hemagglutinin or neuraminadase, newcastle disease virus fusion, infectious bursal disease virus VP2, infectious bursal disease virus VP3, infectious bursal disease virus VP4, infectious bursal disease virus polyprotein, infectious bronchitis virus spike, infectious bronchitis virus matrix, and chick anemia virus.

12. The recombinant **fowlpox** virus of claim 3, further comprising a foreign DNA sequence which encodes a detectable marker.

13. The recombinant **fowlpox** virus of claim 12, wherein the detectable marker is E. coli beta-galactosidase.

14. The recombinant **fowlpox** virus of claim 12, wherein the detectable marker is E. coli beta-glucuronidase.

15. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA encodes a **cytokine**.

is chicken myelomonocytic growth factor (cMGF) or chicken **interferon** (cIFN).

17. The recombinant **fowlpox** virus of claim 15, wherein the **cytokine** is selected from the group consisting of: interleukin-2, interleukin-6, interleukin-12, interferons, granulocyte-macrophage colony stimulating factors, and interleukin receptors.

18. The recombinant **fowlpox** virus of claim 1, wherein the foreign DNA is under control of a promoter.

19. The recombinant **fowlpox** virus of claim 18, wherein the foreign DNA is under control of an endogenous upstream poxvirus promoter.

20. The recombinant **fowlpox** virus of claim 18, wherein the foreign DNA is under control of a heterologous upstream promoter.

21. The recombinant **fowlpox** virus of claim 18, wherein the promoter is a synthetic pox viral promoter.

22. The recombinant **fowlpox** virus of claim 21, wherein the synthetic pox viral promoter is selected from the group consisting of: pox synthetic late promoter 1, pox synthetic late promoter 2 early promoter 2, pox synthetic early promoter 1 late promoter 2, and pox synthetic early promoter 1.

23. A vaccine which comprises an effective immunizing amount of the recombinant **fowlpox** virus of claim 1 and a suitable carrier.

24. A method of immunizing an animal against an animal pathogen which comprises administering to the animal an effective immunizing dose of the vaccine of claim 23.

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=> file medline
COST IN U.S. DOLLARS                              SINCE FILE     TOTAL
                                                       ENTRY   SESSION
FULL ESTIMATED COST                                   126.02    126.23

FILE 'MEDLINE' ENTERED AT 15:47:46 ON 06 MAR 2006

 FILE LAST UPDATED: 4 MAR 2006 (20060304/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s (fowlpox or TROVAC)
           558 FOWLPOX
             3 TROVAC
L6         558 (FOWLPOX OR TROVAC)

=> s l6 and (HIV or Gag)
        156465 HIV
         12161 GAG
L7          40 L6 AND (HIV OR GAG)

=> s l7 and py<2000
      12399668 PY<2000
                 (PY<20000000)
L8          11 L7 AND PY<2000

=> d l8,cbib,ab,1-11

L8   ANSWER 1 OF 11     MEDLINE on STN
2000388389.    PubMed ID: 10901858.   [Antiviral vaccines].    Les vaccins
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Virologie, Lyon, France.. mgirard@ens-bma.cnrs.fr) . Medecine tropicale : revue du Corps de sante colonial, **(1999)** Vol. 59, No. 4 Pt 2, pp. 522-6. Journal code: 8710146. ISSN: 0025-682X. Pub. country: France. Language: French.

AB Vaccination has been successful in controlling numerous diseases in man and animals. Smallpox has been eradicated and poliomyelitis is on the verge of being eradicated. The traditional immunization arsenal includes vaccines using live, attenuated, and inactivated organisms. DNA recombinant technology has added two new types of vaccines, i.e. subunit vaccines based on purified antigens produced by genetic engineering in bacterial, yeast, or animal-cell cultures and live recombinant vaccines based on attenuated bacterial or viral vectors. Currently the best known examples of these new vaccines are those using poxvirus vectors (vaccinia virus, canarypox virus, or **fowlpox** virus) but new vectors are under development. Another application for genetic engineering in the field of vaccinology is the development of DNA vaccines using naked plasmid DNA. This technique has achieved remarkable results in small rodents but its efficacy, safety, and feasibility in man has yet to be demonstrated. Numerous studies are now under way to improve the process. In the field of synthetic vaccines, lipopeptides have shown promise for induction of cell immune response. Development of vaccines for administration by the oral or nasal route may one day revolutionize vaccination techniques. However, effective vaccines against hepatitis C and **HIV** have stalled in the face of the complexity and pathophysiology of these diseases. These are the greatest challenges confronting scientists at the dawn of the new millennium.

L8 ANSWER 2 OF 11 MEDLINE on STN

1999209985. PubMed ID: 10195610. Humoral and cellular immunity induced by antigens adjuvanted with colloidal iron hydroxide. Leibl H; Tomasits R; Bruhl P; Kerschbaum A; Eibl M M; Mannhalter J W. (Department of Immunological Research, Immuno AG, Vienna, Austria.) Vaccine, **(1999 Mar 5)** Vol. 17, No. 9-10, pp. 1017-23. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The immunopotentiating activities of colloidal iron hydroxide, a novel, experimental mineral adjuvant, and of aluminium hydroxide. the licensed adjuvant for human vaccines, were compared. Our studies revealed that colloidal iron hydroxide and aluminium hydroxide behaved comparably with respect to supporting induction of an antibody response to tetanus toxoid. Furthermore, mice immunized with both, the experimental vaccine (tick-borne encephalitis virus (TBEV) antigen adsorbed to colloidal iron hydroxide) or with a commercially available TBEV vaccine (adjuvanted with aluminium hydroxide), developed long-lasting antibody responses which protected the animals from TBEV infection even one year after vaccination. The use of colloidal iron hydroxide as adjuvant had the additional advantage to reproducibly support induction of **HIV**-1 envelope-specific cytotoxic T lymphocytes (CTL), when used as adjuvant for a **HIV**-1 env-carrying recombinant **fowlpox** virus and being applied via the subcutaneous route. Aluminium hydroxide was much less active in this respect. Non-adjuvanted recombinant **fowlpox** elicited CTLs only when given intravenously or intraperitoneally, vaccination routes considered not to be suitable for routine use in humans. Further studies to evaluate the use of colloidal iron as possible alternative and/or supplement for routinely used mineral adjuvants may therefore be warranted.

L8 ANSWER 3 OF 11 MEDLINE on STN

1999030931. PubMed ID: 9811759. Enhanced T-cell immunogenicity and protective efficacy of a human immunodeficiency virus type 1 vaccine regimen consisting of consecutive priming with DNA and boosting with recombinant **fowlpox** virus. Kent S J; Zhao A; Best S J; Chandler J D; Boyle D B; Ramshaw I A. (AIDS Pathogenesis Research Unit, Macfarlane Burnet Centre for Medical Research, Fairfield 3078, Victoria, Australia.. kent@burnet.edu.au) . Journal of virology, **(1998 Dec)** Vol. 72, No. 12, pp. 10180-8. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The induction of human immunodeficiency virus (**HIV**)-specific T-cell responses is widely seen as critical to the development of effective immunity to **HIV** type 1 (**HIV**-1). Plasmid DNA and recombinant **fowlpox** virus (rFPV) vaccines are among the most promising safe **HIV**-1 vaccine candidates. However, the immunity induced by either vaccine alone may be insufficient to provide durable protection against **HIV**-1 infection. We evaluated a consecutive immunization strategy involving priming with DNA and boosting with rFPV vaccines encoding common **HIV**-1 antigens. In mice, this approach induced greater **HIV**-1-specific immunity than either vector alone and protected mice from challenge with a recombinant vaccinia virus expressing **HIV**-1 antigens. In macaques, a dramatic boosting effect on DNA vaccine-primed **HIV**-1-specific helper and cytotoxic T-lymphocyte responses, but a decline in **HIV**-1 antibody titers, was observed following rFPV immunization. The vaccine regimen protected macaques from an intravenous **HIV**-1 challenge, with the resistance most likely mediated by T-cell responses. These studies suggest a safe strategy for the enhanced generation of T-cell-mediated protective

L8 ANSWER 4 OF 11 MEDLINE on STN

1998418739. PubMed ID: 9747943. The role of type-1 and type-2 T-helper immune responses in **HIV**-1 vaccine protection. Heeney J L; van Gils M E; van der Meide P; de Giuli Morghen C; Ghioni C; Gimelli M; Raddelli A; Davis D; Akerblom L; Morein B. (Department of Virology, Biomedical Primate Research Center, Rijswijk, The Netherlands.. heeney@bprc.nl) . Journal of medical primatology, **(1998 Apr-Jun)** Vol. 27, No. 2-3, pp. 50-8. Journal code: 0320626. ISSN: 0047-2565. Pub. country: Denmark. Language: English.

AB The dichotomy of type-1 and type-2 T-helper (Th) immune responses is thought to be an obstacle to develop Human immunodeficiency virus-type- (**HIV**-1) vaccines capable of inducing effective cellular as well as humoral immune responses. Macaca mulatta were immunized using two different **HIV**-1sf2 envelope vaccine strategies, based on either immune-stimulating complexes (ISCOM) or chimeric **Fowlpox** (FP) vaccines. One month following the third immunization all animals were heterologously challenged with simian/human immunodeficiency virus (SHIVsf13). Vaccinated monkeys, which were protected had the highest levels of both type-1 and type-2 **HIV**-1 specific T-helper cell (Th) responses in addition to the highest homologous and heterogenous virus neutralizing antibodies. To determine how long Th responses persisted and if they correlated with protection, animals were rechallenged after waiting for four months without re-boosting. Macaques which maintained the highest gp120-specific type-1 (IFN-gamma) responses were protected, while there was evidence of viral clearance in two others. These findings demonstrate the importance of both or mixed type-1 and type-2 Th responses in **HIV**-1 vaccine induced immunity while suggesting a possible role of persistent type-1 responses in maintaining protective immunity over time.

L8 ANSWER 5 OF 11 MEDLINE on STN

1998225996. PubMed ID: 9565531. Viruses have many ways to be unwelcome guests. Balter M. Science, **(1998 Apr 10)** Vol. 280, No. 5361, pp. 204-5. Journal code: 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.

L8 ANSWER 6 OF 11 MEDLINE on STN

97461115. PubMed ID: 9315482. DNA vaccination against virus infection and enhancement of antiviral immunity following consecutive immunization with DNA and viral vectors. Ramsay A J; Leong K H; Ramshaw I A. (Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University, Canberra, Australia.. Alistair.Ramsay@anu.edu.au) . Immunology and cell biology, **(1997 Aug)** Vol. 75, No. 4, pp. 382-8. Ref: 55. Journal code: 8706300. ISSN: 0818-9641. Pub. country: Australia. Language: English.

AB Recent demonstrations of the immunogenicity of antigens encoded in DNA plasmids following delivery by various routes have heralded a new era in vaccine development. In this article, we review progress in DNA-based antiviral immunoprophylaxis. Preclinical studies have already established the immunogenicity of DNA plasmids encoding protective antigens from a wide variety of viral pathogens and work published in recent months has raised real prospects of broadly protective DNA vaccination against infections with influenza virus and **HIV**. We also describe a consecutive immunization protocol consisting of a priming dose of vaccine antigen encoded in DNA plasmids followed by a booster with the same antigen encoded in recombinant **fowlpox** virus vectors. We have used this strategy to generate protective antiviral cell-mediated immunity and sustained, high-level antibody responses both systemically and at mucosae, and to elucidate immunological mechanisms underlying the development of immunity to antigens delivered in DNA vectors.

L8 ANSWER 7 OF 11 MEDLINE on STN

97030197. PubMed ID: 8876138. Applications of pox virus vectors to vaccination: an update. Paoletti E. Proceedings of the National Academy of Sciences of the United States of America, **(1996 Oct 15)** Vol. 93, No. 21, pp. 11349-53. Ref: 34. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Recombinant pox viruses have been generated for vaccination against heterologous pathogens. Amongst these, the following are notable examples. (i) The engineering of the Copenhagen strain of vaccinia virus to express the rabies virus glycoprotein. When applied in baits, this recombinant has been shown to vaccinate the red fox in Europe and raccoons in the United States, stemming the spread of rabies virus infection in the wild. (ii) A **fowlpox**-based recombinant expressing the Newcastle disease virus fusion and hemagglutinin glycoproteins has been shown to protect commercial broiler chickens for their lifetime when the vaccine was administered at 1 day of age, even in the presence of maternal immunity against either the Newcastle disease virus or the pox vector. (iii) Recombinants of canarypox virus, which is restricted for replication to avian species, have provided protection against rabies virus challenge in cats and dogs, against canine distemper virus, feline leukemia virus, and equine influenza virus disease. In humans, canarypox virus-based recombinants expressing antigens from rabies virus, Japanese encephalitis

attenuated vaccinia derivative, NYVAC, has been engineered to express antigens from both animal and human pathogens. Safety and immunogenicity of NYVAC-based recombinants expressing the rabies virus glycoprotein, a polyprotein from Japanese encephalitis virus, and seven antigens from Plasmodium falciparum have been demonstrated to be safe and immunogenic in early human vaccine studies.

L8 ANSWER 8 OF 11 MEDLINE on STN

95091060. PubMed ID: 7998421. Humoral and cell-mediated immunity in rabbits immunized with live non-replicating avipox recombinants expressing the **HIV**-1SF2 env gene. Radaelli A; Gimelli M; Cremonesi C; Scarpini C; De Giuli Morghen C. (Institute of Pharmacological Sciences, University of Milano, Italy.) Vaccine, **(1994 Sep)** Vol. 12, No. 12, pp. 1110-7. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The canarypox (CP) and **fowlpox** (FP) viruses, which are unable to replicate productively in non-avian species, have been utilized as live vectors carrying the **HIV**-1SF2 env gene with the putative immunosuppressive (IS) region complete (CPIS+ and FPIS+) or deleted (CPIS- and FPIS-). To determine if these avipox-env recombinants could be utilized to elicit a specific immune response against **HIV**-1, six groups of rabbits were immunized with CPIS+, CPIS-, FPIS+, FPIS- constructs or their non-engineered wild-type CPwt or FPwt counterparts. After a primary inoculation and successive boosters, env-specific humoral and cell-mediated immunity were demonstrated by ELISA, immunoblots and lymphoproliferation assays. Antibody titres and neutralization activities were higher in CP- than FP-inoculated rabbits, the CPIS+ always showing a similar immunogenic capacity to CPIS-. Evidence is also presented indicating that rabbit sera possess group-specific antibodies, which were, however, unable to cross-neutralize divergent **HIV**-1 strains. Although the protective capacity against **HIV**-1 experimental infection has not yet been determined in these animals, our results suggest that these recombinants might represent promising and safer candidate vaccines against **HIV**-1.

L8 ANSWER 9 OF 11 MEDLINE on STN

95091059. PubMed ID: 7998420. Expression of **HIV**-1 envelope gene by recombinant avipox viruses. Radaelli A; De Giuli Morghen C. (Institute of Pharmacological Sciences, University of Milano, Italy.) Vaccine, **(1994 Sep)** Vol. 12, No. 12, pp. 1101-9. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Recombinant canarypox (CP) and **fowlpox** (FP) viruses that contained two forms of the **HIV**-1 (SF2 strain) env gene were engineered and their expression analysed in chick, simian and human cells. These vectors can efficiently replicate in avian but not in mammalian cells, in which infection is abortive. The two forms, consisting of the entire env open reading frame (IS+) or of the same gene lacking the putative immunosuppressive (IS-) region (amino acids 583-599), were individually inserted into the two virus vector backgrounds. In order to avoid premature transcription termination of the foreign gene and to improve protein expression, a mutagenesis was also performed within the T5NT motif without altering the amino acid sequence. By immunoprecipitation analyses, cells infected with CP and FP recombinants expressed **HIV**-1 env polypeptides of the appropriate molecular weight. We observed that the gp160 precursor was proteolytically cleaved except in MRC-5 cells infected with the IS- recombinants and that these polypeptides were glycosylated. Further analysis of these recombinant viruses by indirect immunofluorescence and syncytia inhibition assays indicated that the gp120 gp41 complex was present on the surface of infected cells, the number of syncytia being significantly lower when cells were infected by the CPIS- or FPIS- recombinants. Moreover, sera of immunized rabbits revealed the presence of specific antibodies in animals inoculated either with CP or with FP recombinants. These new constructs, which are unable to support a productive infection in human cells, might therefore also be a good anti-**HIV**-1 candidate vaccine in seropositive hosts.

L8 ANSWER 10 OF 11 MEDLINE on STN

95000927. PubMed ID: 7917517. Analysis of cytotoxic T lymphocyte responses to SIV proteins in SIV-infected macaques using antigen-specific stimulation with recombinant vaccinia and fowl poxviruses. Kent S J; Stallard V; Corey L; Hu S L; Morton W R; Gritz L; Panicali D L; Greenberg P D. (Department of Medicine, University of Washington, Seattle 98195.) AIDS research and human retroviruses, **(1994 May)** Vol. 10, No. 5, pp. 551-60. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Methods to analyze CD8+ CTL responses to simian immunodeficiency virus (SIV)-encoded proteins are essential to understand lentivirus immunopathogenesis and protective immune responses. Recombinant infectious shuttle vectors are useful for analyzing CTL responses to many viruses, including **HIV**. Therefore, CTL responses in SIV-infected Macaca fascicularis to SIV env and SIV **gag**/pol were evaluated using specific antigen stimulation with recombinant vaccinia (rVV) and fowl poxviruses

SIV-infected animals were stimulated with autologous cells infected with rVV expressing SIV env/**gag**/pol, and CTLs specific for SIV env and for SIV **gag**/pol were detected by testing for lytic activity in target cells expressing these genes separately. Lymphocyte subset purifications from the effector population demonstrated that the CTL response was mediated by CD8+ cells, and the use of brefeldin A to selectively block antigen presentation in association with MHC class I products affirmed this cytolytic activity was class I restricted. The use of rVV to analyze responses to SIV genes is potentially problematic in hosts immunized to vaccinia. Fowl poxvirus is an alternative virus that has many of the molecular advantages of vaccinia virus but is genomically distinct. Therefore, the ability of rFPV to expand and detect SIV-specific CTLs was evaluated. Although there was no cytopathic effect following infection with rFPV, macaque cells infected with this vector did express rFPV gene products, and could be used as stimulator and target cells to detect SIV-specific CD8+ CTLs. The results suggest that these recombinant viral vectors can be used to specifically stimulate CD8+, MHC class I-restricted CTLs reactive to SIV proteins, and should facilitate evaluating CTL responses in both SIV-infected animals and animals vaccinated against SIV.

L8 ANSWER 11 OF 11 MEDLINE on STN
92256049. PubMed ID: 1667477. Formation of lentivirus particles by mammalian cells infected with recombinant **fowlpox** virus. Jenkins S; Gritz L; Fedor C H; O'Neill E M; Cohen L K; Panicali D L. (Therion Biologics Corporation, Cambridge, MA 02142.) AIDS research and human retroviruses, **(1991 Dec)** Vol. 7, No. 12, pp. 991-8. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.
AB Recombinant **fowlpox** viruses (FPV) containing the env or **gag**-pol genes of simian immunodeficiency virus from macaques (SIVmac) were constructed. The env, **gag**, and pol-encoded polypeptides were efficiently expressed and processed in avian cells productively infected with FPV as well as in mammalian cells, in which FPV infection is abortive. In addition, the recombinant FPV expressing the **gag**-pol genes directed the formation of defective, lentivirus-like particles which were released into the culture medium of infected cells. Coinfection of cells with the env and **gag**-pol recombinant viruses resulted in the generation of particles containing SIVmac envelope glycoprotein. The applications of this system to vaccine development are discussed.

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     (FILE 'HOME' ENTERED AT 15:39:03 ON 06 MAR 2006)

     FILE 'USPATFULL' ENTERED AT 15:39:18 ON 06 MAR 2006
L1           116 S (FOWLPOX/CLM OR TROVAC/CLM)
L2            53 S L1 AND AY<2000
L3             6 S L2 AND (HIV/CLM OR GAG/CLM)
L4            12 S L1 AND (TROVAC/CLM)
L5            15 S L1 AND (CYTOKINE/CLM OR INTERFERON/CLM)

     FILE 'MEDLINE' ENTERED AT 15:47:46 ON 06 MAR 2006
L6           558 S (FOWLPOX OR TROVAC)
L7            40 S L6 AND (HIV OR GAG)
L8            11 S L7 AND PY<2000

=> s l6 and interferon
         91328 INTERFERON
L9           39 L6 AND INTERFERON

=> s l9 and py<2000
      12399668 PY<2000
                (PY<20000000)
L10          11 L9 AND PY<2000

=> s l10 not l8
L11          10 L10 NOT L8

=> d l11,cbib,ab,1-10

L11 ANSWER 1 OF 10 MEDLINE on STN
1999451176. PubMed ID: 10519931. Embryo vaccination of turkeys against Newcastle disease infection with recombinant fowlpox virus constructs containing interferons as adjuvants. Rautenschlein S; Sharma J M; Winslow B J; McMillen J; Junker D; Cochran M. (Department of Veterinary PathoBiology, College of Veterinary Medicine, University of Minnesota, St. Paul, MN 55108, USA. ) Vaccine, (1999 Oct 14) Vol. 18, No. 5-6, pp. 426-33. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Recombinant fowlpox viruses (rFPV) expressing the fusion and hemagglutinin-neuraminidase glycoproteins of Newcastle disease virus (NDV) as well as chicken type I interferon (IFN) or type II IFN were used to
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changes in the hatchability, survival rate, performance and weight gain were observed after vaccination with the rFPV vaccines in comparison to diluent-inoculated embryos. The rFPV-NDV-IFN-II construct induced the onset of anti-NDV antibody production in SPF birds at one week post hatch, one week earlier than other vaccine constructs. Three to five weeks post hatch, the turkeys were challenged with the neurotropic velogenic NDV strain Texas GB (NDV-GB-Tx). The rFPV-NDV-IFN-II construct was the most protective vaccine against NDV. rFPV vaccines significantly ($p<0.05$) suppressed the mitogenic response of peripheral blood leukocytes in vaccinated turkeys in comparison to placebo inoculated controls at 25 days post vaccination. Birds vaccinated with rFPV-NDV-IFN-I construct did not have an inhibition in the mitogenic response.

L11 ANSWER 2 OF 10 MEDLINE on STN

1999388410. PubMed ID: 10457199. Use of recombinant viruses to deliver cytokines influencing the course of experimental bacterial infection. Cheers C; Janas M; Ramsay A; Ramshaw I. (Department of Microbiology and Immunology, University of Melbourne, Parkville, Victoria, Australia.) Immunology and cell biology, **(1999 Aug)** Vol. 77, No. 4, pp. 324-30. Journal code: 8706300. ISSN: 0818-9641. Pub. country: Australia. Language: English.

AB The feasibility of using viral constructs expressing cytokine genes to influence the course of bacterial infection was tested in mice. The mice were first infected with vaccinia or **fowlpox** viruses expressing the cytokine of interest, then challenged with the facultative intracellular bacterial pathogen Listeria monocytogenes. The course of infection was assessed by subsequent bacterial counts. Expression of IFN-gamma or TNF was protective. Vaccinia virus was more efficient at delivering IFN-gamma-mediated protection than was **fowlpox** virus, which is unable to proliferate in mammalian cells. The effect of vaccinia-IFN-gamma was more apparent in the liver, where vaccinia proliferates to high titres (> 109), than in the spleen, where only 103 vaccinia were isolated. Vaccinia virus expressing IL-4 exacerbated infection. Interleukin-4 exacerbation was T cell independent and was reflected in the failure of macrophage activation, possibly due to suppression of NK cells, which are a source of IFN-gamma early in infection. The clear indication of protection by some cytokines in this prophylactic model appears to justify further study of the therapeutic effects of cytokine-expressing viruses in chronic bacterial infections, especially where a cytokine defect is suspected.

L11 ANSWER 3 OF 10 MEDLINE on STN

1999177560. PubMed ID: 10077834. Induction of humoral and cellular immune responses in mice by a recombinant **fowlpox** virus expressing the E2 protein of bovine viral diarrhea virus. Mehdy Elahi S; Bergeron J; Nagy E; Talbot B G; Harpin S; Shen S H; Elazhary Y. (Virology Section, Faculty of Veterinary Medicine, University of Montreal, Saint-Hyacinthe, Que., Canada.) FEMS microbiology letters, **(1999 Feb 15)** Vol. 171, No. 2, pp. 107-14. Journal code: 7705721. ISSN: 0378-1097. Pub. country: Netherlands. Language: English.

AB A recombinant **fowlpox** virus (rFPV/E2) expressing the E2 protein of bovine viral diarrhea virus (BVDV) was constructed and characterized. Mice were immunized with recombinant virus and both humoral and cellular immune responses were studied. rFPV/E2 induced BVDV-specific antibodies which were detected by ELISA. In addition, mouse sera were shown to neutralize BVDV. A cytokine ELISA assay revealed that mice vaccinated with rFPV/E2 induced 7-fold more **interferon**-gamma than parental **fowlpox** virus.

L11 ANSWER 4 OF 10 MEDLINE on STN

1998377674. PubMed ID: 9711795. Recombinant **fowlpox** viruses coexpressing chicken type I IFN and Newcastle disease virus HN and F genes: influence of IFN on protective efficacy and humoral responses of chickens following in ovo or post-hatch administration of recombinant viruses. Karaca K; Sharma J M; Winslow B J; Junker D E; Reddy S; Cochran M; McMillen J. (Department of Pathobiology, College of Veterinary Medicine, University of Minnesota, St. Paul 55108, USA.) Vaccine, **(1998 Oct)** Vol. 16, No. 16, pp. 1496-503. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB We have constructed recombinant (r) fowl pox viruses (FPVs) coexpressing chicken type I **interferon** (IFN) and/or hemagglutinin-neuraminidase (HN) and fusion (F) proteins of Newcastle disease virus (NDV). We administered rFPVs and FPV into embryonated chicken eggs at 17 days of embryonation or in chickens after hatch. Administration of FPV or rFPVs did not influence hatchability and survival of hatched chicks. In ovo or after hatch vaccination of chickens with the recombinant viruses resulted in protection against challenge with virulent FPV and NDV. Chickens vaccinated with FPV or FPV-NDV recombinant had significantly lower body weight 2 weeks following vaccination. This loss in body weight was not detected in chickens receiving FPV-IFN and FPV-NDV-IFN recombinants. Chickens vaccinated with FPV coexpressing IFN and NDV genes produced less antibodies against NDV in comparison with chickens vaccinated with FPV expressing NDV genes.

L11 ANSWER 5 OF 10 MEDLINE on STN

1998320559. PubMed ID: 9656454. Potential use of cytokine therapy in poultry. Lowenthal J W; York J J; O'Neil T E; Steven R A; Strom D G; Digby M R. (CSIRO Division of Animal Health, Australian Animal Health Laboratory, Geelong, Victoria, Australia.. john.Lowenthal@aahl.dah.csiro.au) . Veterinary immunology and immunopathology, **(1998 May 15)** Vol. 63, No. 1-2, pp. 191-8. Journal code: 8002006. ISSN: 0165-2427. Pub. country: Netherlands. Language: English.

AB Newly hatched chickens are highly susceptible to infection during the first 2 weeks of life. The utilisation of cytokines as therapeutic agents in livestock animals, in particular poultry, has become more feasible with the recent cloning of cytokine genes and the progression of new technologies such as live vectors. We have constructed a live recombinant **fowlpox** virus (FPV) that expresses chicken myelomonocytic growth factor (fp/cMGF). Administration of fp/cMGF to chicks resulted in a marked and sustained increase in the number of circulating blood monocytes as well as an increase in their state of activation, as measured by enhanced phagocytic activity and elevated production of nitric oxide. We have recently cloned the gene for chicken **interferon**-gamma (ChIFN-gamma). Recombinant ChIFN-gamma was capable of protecting chick fibroblasts from undergoing virus-mediated lysis and induced nitrite secretion from chicken macrophages in vitro. Preliminary vaccination trials have indicated that co-administration of ChIFN-gamma with antigen (sheep red blood cells) resulted in enhanced secondary (IgG) antibody responses and allowed a 10-fold lower dose of antigen to be used. Furthermore, administration of ChIFN-gamma resulted in enhanced weight gain in chicks and improved their resistance to disease challenge. The ability of cytokines to combat infection and enhance vaccine efficacy makes them excellent candidates as a therapeutic agents and adjuvants.

L11 ANSWER 6 OF 10 MEDLINE on STN

1998185398. PubMed ID: 9524710. Use of recombinant poxviruses to stimulate anti-melanoma T cell reactivity. Kim C J; Cormier J; Roden M; Gritz L; Mazzara G P; Fetsch P; Hijazi Y; Lee K H; Rosenberg S A; Marincola F M. (Division of Clinical Sciences, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.) Annals of surgical oncology : the official journal of the Society of Surgical Oncology, **(1998 Jan-Feb)** Vol. 5, No. 1, pp. 64-76. Journal code: 9420840. ISSN: 1068-9265. Pub. country: United States. Language: English.

AB BACKGROUND: Dendritic cells (DC) are potent professional antigen-presenting cells that can activate naive T lymphocytes and initiate cellular immune responses. As adjuvants, DC may be useful for enhancing immunogenicity and mediating tumor regression. Endogenous expression of antigen by DC could offer the potential advantage of allowing prolonged constitutive presentation of endogenously processed epitopes and exploitation of multiple restriction elements for the presentation of the same antigen. METHODS: DC were prepared from the peripheral blood of HLA A*0201 patients with metastatic melanoma in the presence of IL-4 (1000 IU/mL) and GMCSF (1000 IU/mL). Recombinant vaccinia and **fowlpox** viruses encoding the hMART-1 gene were constructed and used to infect DC. The efficiency of infection and expression of the MART-1 antigen were assessed by immunohistochemistry and intracellular FACS analyses. Cytotoxic lymphocytes (CTL) were generated by the stimulation of CD8+ T cells, with DC expressing the recombinant gene. Reactivity of the CTL was determined at weeks 1 and 2 by the amount of IFN-gamma released. RESULTS: DC were infected with recombinant poxviruses and demonstrated specific melanoma antigen expression by immunohistochemistry, immunofluorescence, and intracellular FACS analysis. The expression by DC of MART-1 MAA after viral infection was sufficient to generate CD8+ T lymphocytes that recognized naturally processed epitopes on tumor cells in 10 of 11 patients. CONCLUSIONS: Human DC are receptive to infection by recombinant poxviruses encoding MAA genes and are capable of efficiently processing and presenting these MAA to cytotoxic T cells. The potential advantage of this approach is the ability to present specific antigen independent of the identification of the epitope or the MHC restriction element. This strategy may be useful for the identification of relevant epitopes for a diverse number of HLA alleles and for active immunization in patients.

L11 ANSWER 7 OF 10 MEDLINE on STN

95056040. PubMed ID: 7966603. Selective induction of immune responses by cytokines coexpressed in recombinant **fowlpox** virus. Leong K H; Ramsay A J; Boyle D B; Ramshaw I A. (Viral Engineering and Cytokine Research Group, John Curtin School of Medical Research, Australian National University, Canberra.) Journal of virology, **(1994 Dec)** Vol. 68, No. 12, pp. 8125-30. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Avipoxviruses have recently been studied as potential vectors for the delivery of heterologous vaccine antigen. Because these viruses abortively infect mammalian cells yet still effectively present encoded foreign genes to the host immune system, they offer a safer but effective alternative to other live virus vectors. We have examined the effect of

responses to a recombinant **fowlpox** virus expressing influenza virus hemagglutinin. The encoded cytokine was expressed for prolonged periods in infected cell culture with little cytopathic effect due to the abortive nature of the infection. In mice, vector-expressed cytokine dramatically altered immune responses induced by the coexpressed hemagglutinin antigen. Expression of interleukin-6 augmented both primary systemic and mucosal antibody responses and primed for enhanced recall responses. In contrast, expression of gamma **interferon** markedly inhibited antibody responses without affecting the generation of cell-mediated immunity. The safety of these constructs was demonstrated in mice with severe combined immunodeficiency, and no side effects due to cytokine expression were observed. In summary, **fowlpox** virus vectors encoding cytokines represent a safe and effective vaccine strategy which may be used to selectively manipulate the immune response.

L11 ANSWER 8 OF 10 MEDLINE on STN

95046484. PubMed ID: 7958066. Enhancing the recognition of tumour associated antigens. Restifo N P; Minev B R; Taggarse A S; McFarland B J; Wang M; Irvine K R. (Surgery Branch, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.) Folia biologica, **(1994)** Vol. 40, No. 1-2, pp. 74-88. Ref: 69. Journal code: 0234640. ISSN: 0015-5500. Pub. country: Czech Republic. Language: English.

AB Activated CD8+ T cells (TCD8+) can directly recognize malignant cells because processed fragments of tumour associated antigens (TAA), 8-10 amino acids in length and complexed with MHC class I molecules, are displayed on tumour cell surfaces. Tumour cells have been genetically modified in a variety of ways in efforts to enhance the immune recognition of TAA. An alternative strategy is the expression of TAA in recombinant or synthetic form. This has been made possible by the recent cloning of TAA recognized by TCD8+. In this communication we review recent work in our own laboratory on the expression of TAA as synthetic peptide, by "naked" plasmid DNA injected intramuscularly or transdermally, and by recombinant viruses including vaccinia (rVV), **fowlpox** (rFV) and adenovirus (rAd). The expression of TAA in recombinant and synthetic forms allows increased control over the quantity, location, and kinetics of TAA presentation and can result in powerful, specific, anti-tumour immune responses.

L11 ANSWER 9 OF 10 MEDLINE on STN

80171583. PubMed ID: 232340. [Nonspecific prophylaxis and therapy of Pseudomonas aeruginosa wound-infections with paramunization using a mouse-model (author's transl)]. Erregerunspezifische Prophylaxe und Therapie von Pseudomonas aeruginosa-Wundinfektionen mittels Paramunisierung im Mausemodell. Mayr A; Himmer B; Baljer G; Sailer J. Zentralblatt fur Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. Erste Abteilung Originale. Reihe A: Medizinische Mikrobiologie und Parasitologie, **(1979 Sep)** Vol. 244, No. 4, pp. 506-14. Journal code: 0331570. ISSN: 0300-9688. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: German.

AB The effectiveness of paramunization as a antigen nonspecific method to activate mechanisms against wound-infections due to Pseudomonas aeruginosa was studied using a model of direct infection of mice with a "mice-pathogenic" Ps. aeruginosa strain on artificially set wounds. Active paramunization by means of a biological inducer "PIND-AVI" (M-HP 438) significantly reduced the mortality rate between treated and placebo animals. The best results were obtained by parenteral prophylactic application. A four times repeated injection of PIND-AVI before the wound-infection reduced the mortality rate from 80% (placebo animals) to 26.6%. Almost equally good results were obtained by clinically useful therapeutic application of the preparation. A four times repeated treatment of the mice after wound infection lead to a decrease of mortality rates from 86.6% to 36.6%. The paramunization inducer PIND-AVI caused no side effect in any of the experiments. The mode of inducer action in Pseudomonas aeruginosa wound infections appears to be complex. Increased phagocytosis by nonspecific opsonisation, increased macrophage activity and concurrent stimulation of the lymphopoetic system could possible occur. On the other hand the nonspecific action of mediators could also play a role due to the inducer stimulated T-cells and cellular antigens of Pseudomonas aeruginosa. However both mechanisms in cooperation with specific and nonspecific humoral factors are probably interacting together. To what extent a simultaneous synthesis resp. release of endogeneous **interferon** plays a role is not known.

L11 ANSWER 10 OF 10 MEDLINE on STN

71018900. PubMed ID: 4319922. **Fowlpox** virus: **interferon** production and sensitivity. Asch B B; Gifford G E. Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N. Y.), **(1970 Oct)** Vol. 135, No. 1, pp. 177-9. Journal code: 7505892. ISSN: 0037-9727. Pub. country: United States. Language: English.